The study of natural history of multiple sclerosis in the Indian perspective: Experience from a Tertiary care hospital.

Dissertation submitted to the Dr.M.G.R.Medical University, Chennai, Tamil Nadu, in fulfillment of the DM –Neurology University examinations in August 2012

CERTIFICATE

This is to certify that the Dissertation titled " The study of natural history of multiple sclerosis in the Indian perspective: Experience from a Tertiary care hospital " the bonafide work of Dr .Subhransu Sekhar Jena submitted in fulfillment of the DM - Neurology examination conducted by the Tamil Nadu Dr. M.G.R Medical University, Chennai, in August 2012

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LIST OF ABBREVIATIONS

CNS- central nervous system

MS- Multiple sclerosis

IDD- Inflammatory demyelinating disorders

NAA- N-acetylaspartate

OCB-Oligoclonal bands

EPs- Evoked potentials

SSEP- somatosensory evoked potential

VEP- visual evoked potential

BAEP- brainstem auditory evoked potentials

MMF-Mycophenolate mofetil

AZT- Azathioprine

INF- Interferon

GA-Glatiramer acetate

EDSS-expanded disability status scale

O.R.- Odd ratio

C.I.- Confidence interval

OSMS- Optico-spinal Multiple Sclerosis

NOSMS- Nonoptico-spinal Multiple Sclerosis

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ABSTRACT

Title- -"The Study of the natural history of multiple sclerosis in the Indian perspective: Experience from a Tertiary care hospital"

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Introduction- Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system, with a wide spectrum of clinical presentation, a disorder which starts as an inflammatory disorder and progresses to a degenerative phase with significant axonopathy. This stresses the importance of initiation of early DMDs. There is a lot of heterogeneity in the type of MS seen in the western and Eastern hemispheres, both in the clinical spectrum, topography of involvement and differences in natural history. However there is a paucity of reports about natural history of MS from India.

Aim/Objective- To study the spectrum, clinical, imaging, electrophysiological and CSF characteristics of Indian MS with respect to outcome and natural history..

Methodology- Retrospective analysis of patients diagnosed to have MS in the Dept. of Neurology at CMC, Vellore, during a period of 12 years (2000-2012). The Clinical data included antecedent events, clinical symptoms and signs, detailed imaging data with MRI, electrophysiological data including evoked potentials, CSF pattern, treatment details and follow up data for response to treatment were entered into a detailed proforma. Information was obtained from the outpatient case records, discharge summaries and follow up. We performed descriptive analyses using the Chi-square and Fisher`s exact tests for categorical variable and the student`s t test for continuous variable. Multiple binary logistic regressions were done for significance.

Results- 157patients with female preponderance were included in the study.114 patients with follow up 6.16 yrs (±6.29) were analyzed for outcome analysis. The most common variety of MS diagnosed was relapsing remitting (RRMS) type (54.1%). Progressive form of MS (PP, SP) were having significant worse outcome (OR-3.51, 95%CI-2.228-7.98, p=0.004) comparing to relapsing MS after analyzing by multiple logistic regression. EDSS of patients at presentation and at final follow up after 6.16±6.29 years was 4.4±1.31 and 4.1±2.31 respectively. During the first presentation, incomplete recovery, polysymptomatic symptoms like motor and sphincter involvement and during the disease course, bowel, bladder, cerebellar and pyramidal affection predict worse outcome. The MRI of brain showing

cerebellar lesion and cerebral atrophy has correlation with disability progression. CSF oligoclonal band was positive in 36.3%. CSF analysis and evoked potential did not predict about outcome. Treatment with Mycophenolate is having good outcome (O.R-0.284(C.I-0.11-0.683) p=0.0051. in univariate analysis. The OSMS group had a better outcome with Mycophenolate when compared to NonOSMS group, suggesting that this probably represents the NMO spectrum.

Conclusion- The present study highlights the regional and racial variations in the clinical, imaging and laboratory profile of multiple sclerosis. There is a definite need for a good marker for disease activity to decide form of DMDs and predict response for treatment outcome.

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Total – 440 words excluding title and name.

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system, thought to result from immune response to myelin with variability in frequency and chronicity. The spectrum of disease course may include an acute isolated attack without recurrence, recurrent exacerabations, or a progressive phase. The impact of acute events is determined by the extent and severity of pathology. Accumulating long-term disability is believed to be determined by the balance between demyelination, remyelination, and axonal loss. Disease course, impact of individual events through out the course, and accumulating long-term disability collectively define disease severity and natural history. Current understanding of MS pathogenesis suggests that axonal damage starts early in MS[1]and that early intervention promises the benefit of preventing long-term disability. Long-term benefit with minimal toxicity is optimized by treating patients at the optimal point in their disease course.

Variation in the prevalence of MS according to geographical location and the modification of clinical features by ethnic factors are well known. Contrary to the previous belief, that MS is rare in India, recent study suggested that the prevalence rate has increased consequent with the availability of MRI imaging, use of modern investigative facilities and increased awareness.[2]

Previous studies have suggested that Indian and Asian patients with MS behave somewhat differently from their western counterparts. They have greater optic nerve and spinal involvement. [2–10]In India, there is an increased prevalence of recurrent acute transverse

myelitis, high incidence of optico-spinal involvement, severe involvement of spinal cord with greater functional disability and less frequent involvement of cerebellum is seen. However there is a paucity of reports about natural history of MS from India.

Two Indian studies have narrated experience of beta interferon[11] and Mitoxantrone[12] recently. Standard of care provided in our hospital is usually IV methylprednisolone for acute attacks and relapses Azathioprine (AZT) and of recently, Mycophenolate mofetil (MMF). The main limitation for the use of DMD like IFN or Glatiramer acetate (GA) has been for the reason of affordability and lack of Insurance coverage for the expenses. We have used interferon in the form of interferon beta-1a in selected patients. Pulse IV methylprednisolone was used in a few selected cases of RRMS, where there were frequent relapses while on AZT, and pulse Cyclophosphamide in some refractory cases. Mitoxantrone has been given for a few patients with progressive MS. On the basis of several, but somewhat conflicting, Class I and II studies, it is considered possible that azathioprine reduces the relapse rate in patients with MS (Type C recommendation).[13]The lack of formulation of IFN and GA, which could be efficacious and cost effective, is mostly for industry driven reasons. Hence, this study was undertaken to look at the clinical spectrum of disease and to look at the natural history of MS in a tertiary level hospital, where DMD like AZT, MMF, and Cyclophosphamide have been used.

AIMS AND OBJECTIVES

Objectives:

To study the clinical profile, imaging, electrophysiological and CSF characteristics with special reference to outcome in a cohort of patients diagnosed to have Multiple Sclerosis in the Department of Neurology at CMC, Vellore, during a period of 12 years (2000-2012).

Outcome

Development of Relapse /disability progression (EDSS) of Multiple Sclerosis as per established Criteriae.

Sub Aims

- To look at the spectrum of clinical presentation of the disease.
- To look at the utility of various electrophysiological tests including multimode evoked potentials in detecting subclinical neuroaxis sites.
- To look for predictors for relapse/recurrence/progressive forms of Multiple sclerosis.

REVIEW OF LITERATURE

HISTORY

The first case of MS, in history dates back to 1433, when a Dutch saint named Lidwina was diagnosed retrospectively. In 1868, Jean-Martin Charcot, a Professor of Neurology at the University of Paris, who has been called "the father of neurology", has described the disease as ***sclerose en plaques***.Beta-interferon 1b (Betaseron) was approved as the first drug to alter the course of MS in 1993. The face of MS has changed considerably over the past 10 years. Several conceptual shifts have occurred in the past decade that have resulted in improved understanding of disease processes that in turn have ultimately advanced patient care.

PATHOGENESIS — MS is a heterogeneous disorder with variable clinical and pathologic features reflecting different pathways to tissue injury. [14]Inflammation, demyelination, and axon degeneration are major pathologic mechanisms.[15]The most widely accepted theory is that MS begins as an inflammatory autoimmune disorder mediated by auto reactive lymphocytes.[14,16] Later, the disease is dominated by microglial activation and chronic neuro degeneration.[15] Myelin reactive T cells are found in MS plaques and in the CSF and peripheral circulation of patients with MS. [17,18]T helper 17-type immune activation, mediated in part by interleukin 23 expression, is associated with active MS lesions.[19–21] The risk of developing MS is associated with certain class I and class II alleles of the major histocompatibility complex (MHC)[22–27], loci that are involved in T-cell activation and regulation. In addition, mounting evidence suggests that the risk of MS is associated with multiple non-MHC susceptibility genes of modest effect (eg, CD6, CLEC16A, IL2RA, IL7R,

IRF8, and TNFRSF1A) [23,25,26].Reduction in MS disease activity has been demonstrated with immunomodulatory drugs that reduce the Th1 immune response (ie, interferon beta), increase the Th2 and Th3 responses (ie, Glatiramer acetate), or block T-cell movement from the blood into the central nervous system (i.e., Natalizumab).An animal model of MS (experimental allergic encephalomyelitis or EAE) can be induced by myelin antigens [28], including myelin basic protein (MBP), proteolipid protein (PLP), myelin associated glycoprotein (MAG), and myelin oligodendrocyte glycoprotein (MOG) [29].In addition to loss of myelin and oligodendrocytes, axonal injury is a prominent pathologic feature of the multiple sclerosis plaque. [1,30–32]Disease progression involves a degenerative phase of cerebral atrophy and axonal loss that is not clearly related to immune mechanisms or inflammation.

EPIDEMIOLOGY AND RISK FACTORS

A systematic review of 28 epidemiologic studies found that, from 1955 to 2000, the estimated female to male ratio of MS incidence increased from 1.4 to 2.3 [33]. The median and mean ages of MS onset are 23.5 and 30 years of age, respectively. The peak age of onset is about five years earlier for women than for men. RRMS tends to have an earlier onset, averaging 25 to 29 years; this may convert to SPMS at a mean age of 40 to 44 years. PPMS have a mean age of onset of 35 to 39 years. The incidence and prevalence of MS varies geographically [34,35]. There is also a widely held belief of an association between latitude and MS, with the risk of MS increasing from south to north.[33] One proposed explanation for the possible association of MS with latitude is that exposure to sunlight may be protective, either because of an effect of ultraviolet radiation or of vitamin D. [36]A number of studies has

suggested an association between smoking and MS.[37] The month of birth has been implicated as a possible risk factor for MS.[38]

CLINICAL FEATURES

The disease has a highly variable pace and many atypical forms. Features highly suggestive of MS are relapses and remissions, onset between ages 15 and 50, optic neuritis, Lhermitte's sign, Internuclear ophthalmoplegia, fatigue, Uhthoff's phenomenon. Presenting symptoms and signs may be either monofocal (consistent with a single lesion) or multifocal (consistent with more than one lesion). Affective disorder occurs in up to two-thirds of patients with MS, and depression is the most common manifestation. Thirty four to 65 percent of patients have cognitive impairment on the basis of neuropsychological testing, and it may be a common event at the onset of MS. The most frequent abnormalities are with abstract conceptualization, recent memory, attention, and speed of information processing. Epilepsy is more common in patients with MS than in the general population, occurring in 2 to 3 percent of patients. Seizures may be either tonic-clonic in nature or partial complex in semilogy.

Analysis of prospectively collected data from a cohort of 195 patients suggests that symptomatic demyelinating events in early RRMS have a tendency to recur in the same location (eg, spinal cord, optic nerve, and brainstem).[39]

Summaries of many studies provide an average figure of 0.4 to 0.6 relapses per year. Relapses tend to be more frequent during the first years of the disease and wane in later years.

In a single centre study that analyzed data from 2587 relapses occurring in 1078 patients during an average follow-up of 7.4 years, relapses causing permanent disability were rare.[40]

DISEASE PATTERN — The pattern and course of MS is categorized as follows[41]:

1. Relapsing remitting (RRMS) - 85 to 90% of MS cases at onset.

2. Secondary progressive (SPMS) - Ultimately develops in most patients with RRMS and causes the greatest amount of neurological disability.

3. Primary progressive (PPMS) – 10% of cases at disease onset.[42]

4. Progressive relapsing (PRMS).

A clinic-based study of 1100 patients found that 66 % had RRMS disease at onset, 15 %PRMS, and 19 % PPMS.[43]

Clinical course can evolve from relapsing to SPMS; 85 percent of patients begin with a relapsing course, but the proportion remaining as relapsing falls steadily, so that only one-half are still relapsing by nine years from onset. Course of MS with onset after the age of 40 years is progressive in over 60 % of patients.[43]

Clinically isolated syndromes — clinically isolated syndromes are single, monosymptomatic attacks compatible with MS (eg, optic neuritis) that can create a diagnostic, and therefore therapeutic, dilemma.

Tumefactive multiple sclerosis — An acute tumor-like MS variant has been described in which some patients with demyelinating disease present with large (>2 cm) acute lesions, often associated with edema or ring enhancement.[44,45] This type of inflammatory demyelinating disease has been termed tumefactive multiple sclerosis, pseudotumoral multiple sclerosis, transitional sclerosis, diffuse myelinoclastic sclerosis, Marburg disease or variant, and Balo concentric sclerosis.

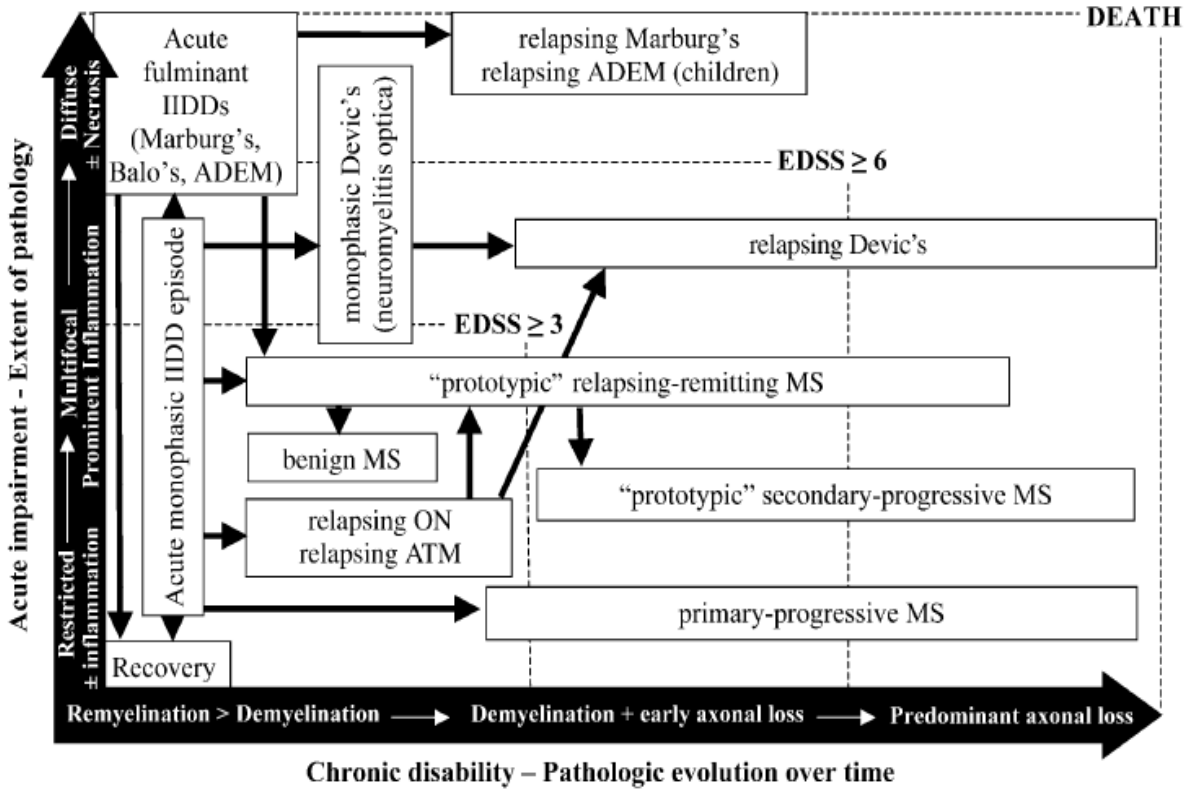


Fig.1-- The balance between inflammation and necrosis and the balance between demyelination,remyelination, and axonal loss on the natural history of IIDDs.[46]

Measures of disease progression — The Kurtzke disability scale, or DSS, and the expanded version (expanded disability status scale, or EDSS) are commonly used indices of clinical disability in MS.[47,48]

The time spent by a patient at a given level of disability varies with the score. The median time spent with a DSS score of 4 or 5 is 1.2 years, while the median time spent at DSS 1 is four years and at DSS 6 three years.[43]

Rate of disability progression — Accumulating evidence suggests that progression of disability in patients with MS is slow,[42,49–53] contrary to the previous studies.[54] One of the largest longitudinal studies followed 2319 patients from British Columbia for 22,723 patient years.[52] Disability scores were prospectively assigned in greater than 95 percent of the patients. The following observations were reported[52]:

- The median time from disease onset to EDSS 6 (cane needed for walking) was 27.9 years; the median age from birth to EDSS 6 was 59 years.

- A primary progressive course was associated with more rapid disease progression than a relapsing course, and was a risk factor in multivariate analysis for time to use of a cane (EDSS 6) from both MS onset (hazard ratio [HR] 2.90, 95% CI 2.39-3.52) and from birth (HR 2.68, 95% CI 2.20-3.26)

- Although men progressed more quickly than women from onset, both men and women required a cane at similar ages (58.8 and 60.1 years), and male sex was not associated with a worse outcome after controlling for other factors

- Onset of symptoms (eg, motor, sensory, optic neuritis, cerebellar, ataxia, or brainstem) did not predict disease progression after controlling for other factors

- A younger age at onset was associated with slower progression, but patients older at onset were consistently older when they progressed to EDSS 6 than patients younger at onset. Similar results were found in a large epidemiology study from France .[55]

Mortality- A longitudinal population-based study from South Wales found that the mean age at death was 65 years.[56]Respiratory diseases or infection was the most common cause of death. The median survival time from symptom onset was 38 years. The standardized mortality ratio was 2.8, suggesting that patients with MS were nearly three times more likely to die prematurely than the general population.

PROGNOSTIC FACTORS — A variety of factors have been identified as possible prognostic indicators in MS that may modify the disease course or predict exacerbations.

Demographic and racial factors

Relapsing versus progressive phase of disease — The relapsing form of MS is generally associated with a better prognosis than progressive disease.[43,50,52] However, once irreversible disability occurred, the time course of progressive disability is similar in the two groups.

Although not firmly established by the existing evidence, there are data suggesting that most patients with relapsing MS will eventually enter a progressive phase of disease.[43,57] The development of a progressive course may be the single most adverse factor influencing prognosis.[54,57–63]

Symptoms at disease onset — Sensory symptoms and Optic Neuritis were thought to have a better prognosis than those with pyramidal, brainstem, and cerebellar symptoms.[43]However, subsequent data suggested that none of these onset symptoms were independent prognostic factors.[52,64]In a systematic review published in May 2005 that evaluated patients with RRMS, bowel and/or bladder symptoms at onset had strong and consistent associations with poor prognosis. Additional factors that predicted long-term disability in RRMS were incomplete recovery from the first attack, a short interval between the first and second attack, and early accumulation of disability.[64]

As compared with monosymptomatic, Polysymptomatic onset was associated with a significantly shorter time to the development of progressive disease.[57]

Lesion Volume — Lesion volume at five years and the change during the first five years of illness correlated more strongly with disability scores at 14 years suggesting that the development of lesions in the early years may have an important influence on long-term disability.[65]

DIAGNOSIS —

The Poser criteria[60](1980) have been supplanted by the McDonald criteria, which were developed in 2001[66] and subsequently revised in 2005[67] and 2010[68].

McDonald criteria — The McDonald criteria is recently revised in 2010 in order to incorporate newer evidence[69–71]and to simplify the use of neuroimaging while preserving the sensitivity and specificity of the criteria.[68]

- **Dissemination in space**- one or more T2 lesions in at least two of four MS-typical regions of the CNS (periventricular, juxtacortical, infratentorial, or spinal cord) or by the development of a further clinical attack implicating a different CNS site. With brainstem or spinal cord syndromes, symptomatic MRI lesions are excluded from the criteria and do not contribute to lesion count.

- **Dissemination in time** -- Simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions at any time, or a new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan, **or** by the development of a second clinical attack.

  For PPMS, the criteria require evidence of the 1 year of disease progression (retrospectively or prospectively determined) plus 2 of the 3 following criteria (with brainstem or spinal cord syndromes, symptomatic MRI lesions are excluded from the criteria and do not contribute to lesion count):

- Dissemination in space **in the brain** based upon >1 T2 lesions in at least 2 of 4 MS-typical regions of the central nervous system (periventricular, juxtacortical, infratentorial, or spinal cord)

- Dissemination in space **in the spinal cord** based upon 2 or more T2 lesions in the cord

- Positive CSF findings with isoelectric focusing evidence of OCBs and/or elevated IgG index

  MS attack (also called a relapse or exacerbation) is defined by the McDonald criteria as patient-reported or objectively observed event typical of an acute inflammatory

demyelinating event in the CNS, and can be either current or historical, with duration of at least 24 hours, in the absence of fever or infection.[68]

Paroxysmal symptoms should consist of multiple episodes occurring less than 24 hours.

For a definite diagnosis of MS to be made, at least one attack must be confirmed by findings on either neurologic examination, VEP response in patients with prior visual disturbance, or MRI consistent with demyelination in CNS region associated with the prior neurologic symptoms.

The McDonald criteria assign diagnostic confidence as follows[68]:

- The diagnosis of "MS" is given if the criteria are fulfilled and there is no better explanation for the clinical presentation
- The diagnosis of "possible MS" is given if MS is suspected but the criteria are not completely met
- The diagnosis of "not MS" is given if another diagnosis better explains the clinical presentation

Magnetic resonance imaging — MRI is the test of choice to support the clinical diagnosis of MS.[72]

Lesion characteristics — The characteristic lesion demonstrated on MRI is the cerebral or spinal plaque. Plaques suggestive of MS are typically found in the periventricular region, corpus callosum, centrum semiovale, and, to a lesser extent, deep white matter structures and basal ganglia. MS plaques usually have an ovoid appearance, and lesions are arranged at right angles to the corpus callosum as if radiating from this area. The plaques appear hyperintense on proton density and T2-weighted studies, and they are hypointense (if visible at all) on T1-weighted images. MRI scanning is more sensitive and specific for predicting evolution to clinically definite MS than other studies such as CT scans, cerebrospinal fluid parameters, or evoked potentials.[73] [70]

Magnetic resonance spectroscopy (MRS) - Chronic MS is associated with a reduction of NAA in comparison to Choline and Creatinine within the brain. A reduced NAA/Cr ratio implies loss of neurons or axons, which is consistent with pathological studies and appears to parallel disability in MS.[74]

Cerebrospinal fluid analysis — A positive CSF is based upon the finding of either oligoclonal bands (OCBs) or by an increased IgG index. An abnormality of CSF IgG production as measured by the IgG index or IgG synthesis rate is found in 90 percent of clinically definite MS patients.[75]The CSF total leukocyte count is normal in two-thirds of patients, exceeds 15 cells/µL in <5 percent, and only rarely exceeds 50 cells/µL.[76]Lymphocytes are the predominant cell type, the vast majority of which are T cells. CSF protein (or albumin) level is usually normal.

Oligoclonal bands — Oligoclonal bands (OCBs) are found in ≥95 percent of patients with clinically definite MS.[77]The presence of OCBs in monosymptomatic patients predicts a significantly higher rate of progression to MS than the absence of bands: 25 versus 9 percent at three years follow-up in one report.[75]However, quantification of OCBs is an insensitive prognostic indicator.[78]

Evoked potentials (EPs) — Detection of a subclinical lesion in a site remote from the region of clinical dysfunction supports a diagnosis of multifocal MS. The three most frequently used EPs are somatosensory (SSEP), visual (VEP), and brainstem auditory evoked potentials (BAEP).

- Patients with clinically definite MS have abnormal VEPs in 85% of cases.[79]

- SSEPs are abnormal in 77% of patients with MS, including approximately one-half of those who do not have sensory signs or symptoms

- BAEP abnormalities are less frequent in MS than VEP or SSEP abnormalities, being present in 67% of patients with MS.

American Academy of Neurology (AAN) states that VERs are probably useful for identifying patients with clinically definite MS, SSEPs are possibly useful, and there is insufficient evidence at this time to recommend BAEP as a useful test for diagnostic purposes.[80]

Differential diagnosis of multiple sclerosis-

Various inflammatory or infectious diseases such as systemic lupus erythematosus, Sjögren's disease, polyarteritis nodosa, Behçet's disease, syphilis, and retroviral diseases may all produce multifocal lesions with or without a relapsing-remitting course. Systemic lupus erythematosus can present as a recurrent neurologic syndrome before the systemic manifestations of this disease appear. Behçet's syndrome is characterized by orogenital ulcerations; multifocal neurologic findings occur in less than one-third of these patients The inherited vasculopathy known as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) can likewise produce a pattern of brain lesions on MRI that can mimic the pattern seen in patients with MS.

TREATMENT---

Treatment of acute exacerbations of multiple sclerosis

1. GLUCOCORTICOIDS — Acute attacks of MS are usually treated with glucocorticoids. 3-7 day courses of IVmethylprednisolone, 0.5 to 1gm daily, with or without a short prednisone taper, are used most commonly.[81,82] On the basis of Class I and Class II studies, glucocorticoid treatment has been demonstrated to have a short-term benefit on the speed of functional recovery in patients with acute attacks of MS. It is appropriate, therefore, to consider for treatment with glucocorticoids any patient with an acute attack of MS (Type A recommendation).[13]

2. PLASMA EXCHANGE - For patients with acute, severe neurologic deficits caused by multiple sclerosis who have a poor response to treatment with high-dose glucocorticoids, plasma exchange is advocated.[83,84]

DISEASE MODIFYING THERAPY-

For patients with RRMS, there are currently seven approved medications that have been shown to alter the natural course of the disease. The FDA approved medications include three beta interferon (IFNb) formulations, beta-1a(30 μg IM weekly), beta-1a(44 μg thrice weekly) and beta-1b (250μg S/C every other day), Glatiramer acetate (GA), Natalizumab and Mitoxantrone and recently oral fingolimod. There is currently no evidence that IFNb, GA and Natalizumab are effective in very aggressive forms of RRMS and progressive disease forms of MS. Mitoxantrone is approved for treatment of secondary progressive MS with worsening relapsing and progressive relapsing disease course.

Mycophenolate (MMF)—It is a potent immunosuppressant that is a selective inhibitor of inosine 5'-monophosphate dehydrogenase type II. Preliminary studies have shown good tolerability and safety when MMF is utilized as monotherapy or in combination with interferons or Glatiramer acetate.[85,86]

Both interferon beta and MMF appeared safe and well tolerated in the majority of patients. There was no difference between MMF therapy and the standard regimen of interferon beta therapy on the primary safety MRI endpoints of the study. However, the MMF group showed a trend towards a lower accumulation of combined active lesions, Gado and T2 lesions when compared with interferon beta.[87]

Azathioprine- Administered at lymphocyte-suppressing doses, is effective in reducing new brain inflammatory lesions and is well tolerated.[88–90]In a meta-analysis of five randomized controlled trials, azathioprine was associated with a statistically significant reduction in the number of relapses during the first, second, and third years of treatment; relative risk reductions for these periods were 20, 23, and 18 percent, respectively. Considering the benefit and harms, azathioprine is a fair alternative to interferon beta for treating MS. A logical next step for future trials would seem the direct comparison of Azathioprine and interferon beta. In fact the direct comparison between these two widely used treatments in MS has not been made.[91]

One small, open-label study found that Azathioprine up to 3 mg/kg per day was well tolerated and reduced the rate of new gadolinium-enhancing brain lesions in patients with RRMS.[88]

Cyclophosphamide- monthly intravenous doses influence the frequency and duration of episodes of relapsing/remitting multiple sclerosis.[92]The RRMS group benefited the most from high dosage cyclophosphamide and had a significant reduction in the flare frequency. According to this trial high dose was found ineffective in SPMS.[93]

DMD therapies have known to have short-and medium-term (2–5 years) benefit in reducing relapses, disability progression, and appearance of new inflammatory lesions on magnetic resonance imaging (MRI).[94–104]It is proposed that the effect of DMD is in initial inflammatory phase not in later degenerative phase. The short duration of the randomized pivotal MS trials have provided little to no information about benefit from such treatment over periods of extended (>5 years) use.

MATERIAL AND METHODS

The inpatient data base of the Department of Neurology at the Christian Medical College, Vellore was searched for patients admitted /evaluated with the diagnosis of Multiple sclerosis during the period of Jan 1, 2000 to 29th Feb 2012 (12 year period) for inclusion in the study. This study is a Clinical Investigator driven study and has been approved by the IRB (No-7521 dated 5.7.2011)

The Clinical data included antecedent events, clinical symptoms and signs, detailed imaging data with MRI, electrophysiological data including evoked potentials, CSF pattern, treatment details and follow up data for response to treatment were entered into a detailed proforma. Information was obtained from the outpatient case records, discharge summaries and follow up.

There were a total number of 157 patients who were evaluated during this period and follow up details were available for114 patients.

INCLUSION CRITERIA-

1. Patients diagnosed to have MS according to Mc Donald`s criteria.[68]
2. Multiple sclerosis with minimum 1 years of follow up were included

EXCLUSION CRITERIA

1. ADEM, opticospinal form of ADEM, postinfectious encephalitis/ encephalomyelitis, acute transverse myelitis (Complete evolution within 24-48

hours with complete transaction without evidence of clinical/subclinical involvement of any site other than cord.)

2. Neuromyelitis optica (Revised diagnostic criteria for NMO published in 2006)[105]
3. Evidence of causes other than inflammatory demyelination on radiological, biochemical and microbiological tests.

The following definitions were used for the various presentations—

1. **Acute presentation**- onset of illness to peak in one week.
2. **Subacute presentation**- onset of illness to peak beyond one week but within one month.
3. **Chronic presentation**- peak beyond one month.
4. **Encephalitis-like presentation** – patients with spectrum of symptoms of fever, headache, altered sensorium, seizures (GTCS or Focal) with / without focal deficits.
5. **Stroke like presentation**- neurological deficit mimicking involvement in a vascular territory without preceding headache or encephalopathy.
6. **Tumour like presentation** – Predominant headache/vomiting/raised ICT features with or without progressive focal deficits.
7. **Optic Neuritis**-unilateral or bilateral painless partial or complete loss of vision with partial or complete recovery, on follow up. No other local pathology of the eye was responsible for the vision loss.

8. **Optico-spinal presentation** – patients who presented with features of diminished vision bilaterally or unilaterally in conjunction with features of cord involvement.
9. **Myelitis** – patients with features suggestive of cord involvement.
10. **Cerebellitis** – patient presented only with cerebellar deficits.

Baseline Evaluation

The Kurtzke Expanded Disabilty Status Scale (EDSS) was recorded for each patient.[48]

Follow up Evaluation

During each visit a detailed history was taken and the finding on clinical examination was recorded with respect to the progression of symptoms or appearance of new signs. EDSS was recorded at each visit. Gadolinium – enhanced MRI of the brain and spine was done as required.

Clinical Relapse: Patient reported symptoms or objectively observed signs typical of an acute inflammatory demyelinating event in the CNS, current or historical, with duration of at least 24 hours, in the absence of fever or infection. Paroxysmal symptoms (historical or current) should however consist of multiple episodes occurring not beyond 24 hours. If a patient had a relapse, the nature of relapse was recorded, MRI was done, Standard therapy for relapse was given and the recovery recorded.

Clinical progression:

It was defined as change in EDSS by one point in the absence of relapse

MRI Technique:

The imaging data were interpreted by consultant radiologist. MRI sequences of the brain like, T1, T2, FLAIR Post Gadolinium (contrast) and cord were studied. In a suspected case of MS, double dose of Gadolinium was used occasionally when an active plaque was suspected.

1) The total number of lesions, their location and size, cerebral atrophy were noted.

2) The images taken during the first episode and subsequent follow up were studied.

3) A detail study and comparison of the scans at admission and last follow up was done.

Progression on MRI

Progression on MRI was defined as the appearance of a new gadolinium –enhancing lesions at a site different from that recorded earlier, appearance of a new T2-W lesion, or increase in the size of an older lesion or brain atrophy.

Comparison of follow up MRI

The MRI done on follow up was compared to the baseline MRI. The laboratory data from Biochemistry, Microbiology and Neurochemistry labs were obtained from the respective department records. CSF cells, Proteins and presence of Oligoclonal bands or raised IgG levels were noted. The specific tests reviewed included bacterial and fungal cultures from the blood and CSF wherever necessary. Vasculitic markers, collagen disease markers,

sarcoidosis were ruled out in all the cases. Seropositivity for HIV was looked for. Multimodal evoked potentials i.e. visual evoked potentials, brainstem auditory evoked potentials and somatosensory evoked potentials (Median and Tibial) reports of all patients were reviewed in the electrophysiology lab. The multimodal evoked potentials were done with Nicolet Bravo model GT 775 machine.

The treatment received at acute presentation and maintenance therapy was also noted from the records. The comparison between various treatment modalities was done.

Statistical Analysis-

We performed descriptive analyses using the Chi-square and Fisher`s exact tests for categorical variable and the student`s t test for continuous variable. Statistically significance was taken to be at the two-tailed 0.05 level. Multiple binary logistic regressions were done for significance. All statistical analyses were performed with the SPSS statistical software package version 16 (SPSS Inc. Chicago, Illinois, USA).

RESULTS

A total of 157 patients fulfilled the criteria for multiple sclerosis during a study period of 12 years. The follow up data was available for 114(72.6%) patients. 146(93%) were adults and 11(7%) were children below the age of 16 years at the time of inclusion in the study.

The observed MS types were RR 85(54.1 %), PP 24(5.3 %), SP47 (29.9 %), PR 1(0.6 %). There is no statistically difference for predlication of MS type with gender. 47(35.6 %) of RRMS patient, during follow up has attained SPMS.

59(37.6 %) patient has Opticospinal syndrome presentation and rest 98(62.4%) has non Opticospinal syndrome. In Opticospinal group 4 patients (2.5%) fits in to NMO spectrum of disorder.

Table -1 Baseline Characteristics of the 157 patients

	Optico-spinal (n=59) (%)	**Nonoptico-spinal (n=98) (%)**	**Total Number (n=157) (%)**
Males	24(40.7%)	47(48%)	71(45.2)
Females	35(59.3)	51(52%)	86(54.8)
Adults	52(88.1)	94(95.9)	146(93)
Children	7(11.9)	4(4.1)	11(7)
Mean age	27.15(±9.71)(R12-51)	30.7(±10.1)(R8-58)	29.38 ±10.09R8-58)
Duration of follow up			
Mean	5.95(±5.56)(R1-24)	6.28(±6.7)(R1-33)	6.16 yrs(±6.29)(R1-33)

The mean age is 29.38 10.09(Range8-58) at the time of inclusion of study. The maximum number of patients 77(49%) are in 16-33 yr age group. At present the mean age is 38.57 11.7(Range 15-70).

71(45.2%)) were males and 86(54.8%) were females in this group. The Female/ Male ratio was 1.21. There was no statistically difference between the ages, gender, and year of follow up among groups.

Table-2 Initial neurologic symptoms

symptoms	No of patients	% of patients
Monosymptomatic	107	68.2
Polysymptomatic	50	31.8
Motor weakness	(Paraparesis-42, Monoparesis-18, Hemiparesis-9, Quadriparesis-3) 72	45.8
Brain stem/Cerebellum	51	32.5
Visual loss	(U/L Vision-36, B/L vision-6) 42	26.7
Sensory symptoms	38	24.2
Sphincter disturbances	12	7.6
Others	11	7

Initial presentation were motor weakness predominates (45.8%) followed by brainstem/cerebellar (32.5%) patients. The asymmetrical onset B/L visual loss was seen in 6 patients. Monosymptomatic presentations were 68.2% while polysymptomatic presentations were 31.8%.

Table-3 Presentation of total patients during the course of illness

Presentation	Optico-spinal(n=59)(%)	Nonoptico-spinal (n=98)(%)	Total Number (n=157) (%)
Acute(<1week)	9(15.3)	14(14.3)	23(14.6)
Sub acute (1wk-1month)	1(1.7)	5(5.1)	6(3.8)
Chronic(> 1 month)	0	21(21.4)	21(13.4)
Temporal profile (Acute,chronic,subacute)	49(83.05)	58(59.1)	107(68.1)
Monosymptomatic	51(86.4)	56(57.1)	107(68.2)
Polysymptomatic	8(13.6)	42(42.9)	50(31.8)
Relapsing recurrent	38(64.4)	47((48)	85(54.1)
Primary progressive	0	24(24.5)	24(15.3)
Secondary progressive	21(35.6)	26(26.5)	47(29.9%)
Progressive relapsing	0	1(1)	1(0.6)

Monosymptomatic presentation was more in Opticospinal group (p=0.000). The Temporal profile (Acute, chronic, sub acute) presentation were present more in Optico-spinal group (p=0.004). Relapsing recurrent MS is more common in Optico-spinal group (p=0.000)

Table-4 Clinical profile of patients during follow up

Variables	Optico-spinal(n=59) (%)	Nonoptico-spinal (n=98)(%)	Total(n=157) (%)	p value
Stroke like	1(1.7)	8(8.2)	9(5.7)	NS
Hemispheric	0	12(12.2)	12(7.6)	0.005
Brain stem dysfunction	11(18.6)	32(32.7)	44(27.4)	NS
Cerebellar dysfunction	16(27.1)	42(42.9)	58(36.9)	0.048
Pyramidal	55(93.2)	81(82.7)	136(86.6)	NS
Sensory	50(84.7)	70(71.4)	120(76.4)	NS
Tumour like	0	2(2)	2(1.3)	NS
Myelitis	58(98.3)	70(71.4)	128(81.5)	0.000
Optic nerve	58(98.3)	34(34.7)	92(58.6)	0.000
Diplopia	20(33.9)	21(21.4)	41(26.1)	NS
Oscillopsia	22(37.3)	21(21.4)	43(27.4)	0.031
Nystagmus	12(20.3)	22(22.4)	34(21.7)	NS

Variables	Optico-spinal(n=59) (%)	Nonoptico-spinal (n=98)(%)	Total(n=157) (%)	p value
INO	1(1.7)	8(8.2)	9(5.7)	NS
Ophthalmoplegia	1(1.7)	12(12.2)	13(8.3)	0.02
Facial Myokymia	0	1(1)	1(0.6)	NS
Facial Spasm	0	3(3.1)	3(1.9)	NS
Lhermitte's	10(16.9)	14(14.3)	24(15.3)	NS
Uhthoff`s	1(1.7)	4(4.1)	5(3.2)	NS
Trigeminal Neuralgia	4(6.8)	4(4.1)	8(5.1)	NS
Parasthesia,Dysthesia	44(74.6)	63(64.3)	107(68.2)	NS
Sensory symp in face	7(11.9)	12(12.2)	19(12.1)	NS
Bladder-UMN	41(69.5)	57(58.2)	98(62.4)	NS
Bladder-LMN	30(50.8)	39(39.8)	69(43.9)	NS
Constipation	27(45.8)	46(46.9)	73(46.5)	NS

Variables	Optico-spinal(n=59) (%)	Nonoptico-spinal (n=98)(%)	Total(n=157) (%)	p value
Fecal Incontinence	6(10.2)	6(6.1)	12(7.6)	NS
Bowel bladder	43(72.9)	61(62.2)	104(66.2)	NS
Sexual Dysfunction	7(11.9)	17(17.3)	24(15.3)	NS
Fatigue	42(71.2)	59(60.2)	101(64.3)	NS
Gait involvement	53(89.8)	84(85.7)	137(87.3)	NS
Limb ataxia	14(23.7)	31(31.6)	45(28.7)	NS
Vertigo	9(15.3)	25(25.5)	34(21.7)	NS
Seizures	3(5.1)	6(6.1)	9(5.7)	NS

NS-Not significant

Hemispheric, cerebellar, ophthalmoplegia were more common in NOSMS, while myelopathy, optic neuropathy were commoner in OSMS.

COURSE OF THE DISEASE-

The follow up data was available for 114(72.6%) patients.

Number of Episodes – 16(14%) had 1 episode, 23(20.2%) had 2 episodes, 41(36%) had 3 episodes and 20(17.5%) had 4 episodes of illness. The annualized relapse rate (ARR) is 0.35 /yr

Mean number of episodes was 3±1.36 in our study. The Range was 8(1-9). The second episode occurred 1.62±1.96 yr (Range0.1-12 yrs) after the first one. The recovery was complete in 109(69.4%) patients after first episode.

MULTIMODAL EVOKED POTENTIALS IN THIS STUDY

- Data is not available in 5 patients. VEP, SSEP Tibial, SSEP Median, BAER, was done in 95.5%, 87.3%, 59.8%, and 43.9% respectively.

- VEP- 59.3% (89/150) had bilateral abnormality; 18.6% (28/150) had unilateral abnormality.

- 67.3% (93/138) had abnormal tibial SSEPs

- 51.1% (48/94) had abnormal median SSEPs.

- 39.1% (27/69) had abnormal BAER findings.

CSF Abnormalities in Study

- 55.4 %(87/157) has CSF cell and protein value within normal range.

Table-5 CSF analysis

	No of patients	**% of patient**
CSF protein 45-90mg%	47	29.9
CSF protein <45mg%	110	70.1
CSF Cells10-25	29	18.5
CSF Cells 25-50	6	3.8
CSF cells<10	122	77.7
OCB present	53	36.3(53/146)
OCB data not available	11	7

In the OSMS and NOSMS the OCB was positive in 39 %(22/56) and 34.4 %(31/19) and there was no statistically difference among groups.

MRI scan Studies

All the patients had abnormalities in the MRI of the brain and 134(85.3%) abnormalities were detected on the spinal cord imaging. > 15 lesions were found in 140(89.2%) patients. Ten (6.4%) patient`s MRI showed spinal cord hyper intensity involving >3 vertebral segments.

Table-6 MRI studies

Sites	No of patients	% of patients
Periventricular	150	95.5
Juxtacortical	147	93.6
Infratentorial	103	65.6
Callosal and Pericallosal lesions	98	62.4
Dawson`s finger	50	31.8
Brain stem	98	62.4
Cerebellum	47	29.9
Cerebellar Peduncle	38	24.2
Thalamus	23	14.6
Basal ganglia	19	12.1
Cervical cord	126	80.3
Thoracic cord	93	59.2
Cervico thoracic cord	80	51
Gadolinium enhancement	48	30.6

The most common location of lesions were periventricular (95.5%), Juxtacortical (93.6%), Infratentorial (65.6%). Dawson`s finger were observed in 31.8%.

The size of brain lesion were <3 cm in 151(96.2 %) patient. 5(3.2 %) has 3-5 cm brain lesion and 1 patient has 6 cm brain lesion.

Follow up MRI was done in mean year of 1.88±2.35 years (Range-0.2-13). The follow up MRI data was not available in 44(28 %) patients. Improvement was noted in 24(21.2 %) patient and worsening in the MRI parameters (increase in number, size, gado enhancement) were observed in 43(38.05 %). There was no appreciable changes were noted in 46(40.7 %)

Cerebral atrophy was noted in 82(52.2 %) patient. The first scan revealed cerebral atrophy in 60 patients and 22 patients in follow up studies. Most common type of atrophy is sub cortical 62/82(75.6 %). Cortical, sub cortical and callosal atrophy was noticed in 20 patients (24.6%)

Table-7 Treatment received in acute phase and as DMDs

Treatment	No of patients	% of patients
Acute treatment-MP	147	93.6
IVIG+ MP	8	5.1
Plasmapheresis	5	3.2
ACTH	1	0.6
Pulse IV Methylprednisolone	68	43.3
Oral steroid	14	8.9
Azathioprine	68	43.3
Mycophenolate	85	54.1
Cyclophosphamide	23	14.6
Mitoxantrone	5	3.2
INF	13	8.3
Glatiramer	4	2.5
Methotrexate	3	1.9

The most common immunomodulatory agent is MMF (54.1%) followed by AZT (43.3%). INF most commonly received was interferon β-1a.

Presently 9.6 %(11/114) patients is not receiving any treatment and 3.5 %(4/114) is taking alternate preparations. The pulse methyl prednisolone (weekly tapering schedule) was given

for mean 15.2±7.5 weeks. Inj cyclophosphamide (700-1000mg/$m^{2)}$ was given as monthly pulses for mean of 10.68±3.3. Earlier the standard of practice was treatment with azathioprine. However the azathioprine was switched over to Mycophenolate in 17.6% (12/68) patients due to clinical worsening.

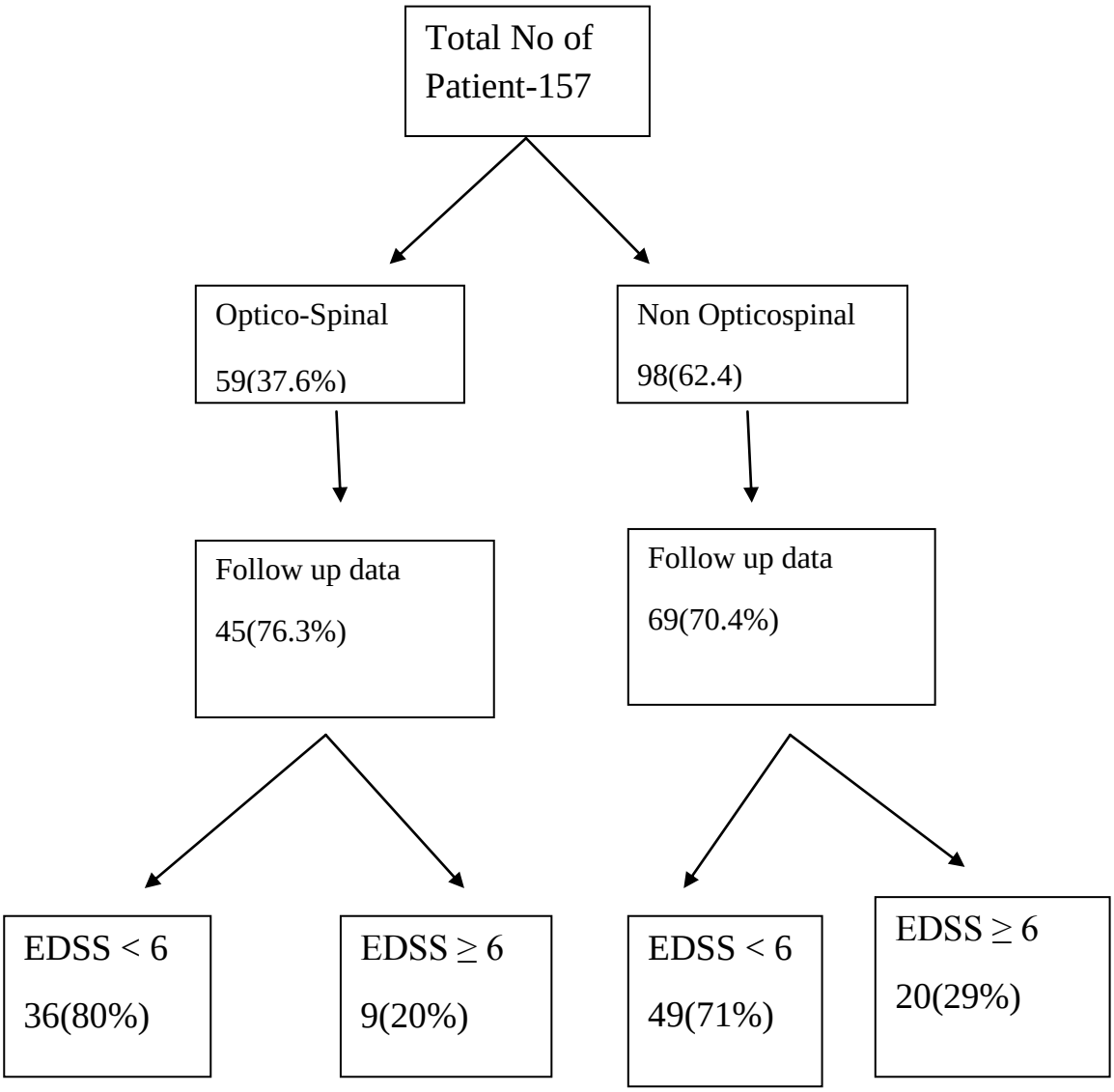
OUTCOME ANALYSIS

The patients presented to us after a mean of 3.8±3.59 yrs (range-0.1-19) following the first episode. EDSS of patients at presentation was with mean 4.4±1.31 (Range 1-8). The mean duration of follow up for 114 patients was 6.16±6.29 years (range 32 years 1-33). During the last follow up the EDSS was mean 4.1±2.31 (range 0-10)

For outcome analysis two groups has been divided based on final follow up EDSS as ≥6 and <6 on basis of requirement of support for ambulation.

In view of Opticospinal syndrome can be of NMO spectrum of disorder and as we have not done NMO antibody for most of the patients, for final outcome analysis we have divided to Opticospinal MS (OSMS) and nonoptico-spinal MS (NOSMS). One patient has death due to accidental cause was not included in the final outcome. One patient has death due to respiratory failure attributable by significant cervico-medullary lesion.

Figure-2 Final outcome analysis



The difference in outcome for OSMS and NOSMS is not stasttically significant as p= 0.282

Table-8.1 Outcome analysis of total patients (n=114)

Out come	EDSS <6 (n=85)		EDSS ≥6 (n=29)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Male	33	33.8	14	48.3	1.471	.62-3.43	.37			
Female(Ref)	52	61.2	15	51.7						
SP+PP	23	27.1	25	86.2	16.4	5.28-53.68	.00	3.51	2.28-79.8	.004
RR(Ref)	62	72.9	4	13.8						
Recovery after 1st episode-complete	67	84.8	13	56.5	.233	.083-.651	.005	.46	.09-2.18	.331
Presenting symp-Motor	28	32.9	15	51.7	2.18	.92-5.14	.075			
Presnting symp-Sphincter disturb	1	1.2	4	13.8	13.44	1.43-125.7	.023			
Polysymptomatic	16	18.8	16	55.2	5.3	2.1-13.2	.000	2.86	.54-15.07	.214
Monosymptomatic(Ref)	69	81.2	13	44.8						
Cerebellar	30	35.3	17	58.6	2.59	1.09-6.15	.030	.264	.042-1.65	.155
U/L ataxia	19	22.4	15	51.7	3.72	1.52-9.05	.004			
Optico-spinal	36	42.4	9	31	0.613	.25-1.501	0.28			

Out come	EDSS <6 (n=85)		EDSS ≥6 (n=29)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Bladder-UMN	48	56.5	24	82.8	3.7	1.28-10.62	.015	1.34	.21-8.57	.752
Bladder- LMN	30	35.3	20	69	4.07	1.65-10.05	.002			
Constipation	32	37.6	21	72.4	4.34	1.65-10.05	.002			
Faecal urge incontinence	2	2.4	4	13.8	6.64	1.14-38.4	.035			
Sexual dysfunction	8	9.4	7	24.1	3.06	1.14-38.4	.05			
Pyramidal affection	69	81.2	28	96.6	6.49	.82-51.32	.076			
MRI-cerebellar lesion	20	23.5	13	44.8	2.64	1.08-6.44	.032	3.23	.703-14.87	.132

During the presentation the symptoms like visual, sensory, brain stem, cerebellar, does not help in predicting worse out come. The analysis for gender, stroke like, brain stem, hemispheric, Optico-spinal, myelitis, tumor like, optic neuropathy, Diplopia, Oscillopsia, Nystagmus, INO, ophthalmoplegia, facial myokymia, facial spasm, facial sensory loss, Lhermitte`s, Uhthoff`s, Trigeminal neuralgia, parasthesia , dysesthesia , fatigue, vertigo, seizures symptom analysis is not having statistically significant difference as $p>0.05$.

Table-8.2 Outcome analysis of total patients (n=114)

Out come	EDSS <6 (n=85)		EDSS ≥6 (n=29)		unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
MRI-Basal ganglia lesion	2	2.4	5	17.2	8.64	1.57-47.4	.013			
MRI-Cerebral atrophy	34	40	25	86.2	9.37	2.99-29.34	0.000	4.508	.78-25.92	.092
Pulse IV MP	50	58.8	14	48.3	1.607	.688-3.75	.273			
Mycophenolate	63	74.1	13	44.8	.284	.11-.683	.005	.993	.236-4.171	.992
Azathioprine	24	28.2	14	48.3	2.37	.996-5.65	.051	2.707	.62-11.81	.185
First EDSS>6	5	5.9	12	41.4	11.29	3.51-36.2	0.000	2.23	.42-11.62	.339
First EDSS<6	80	94.1	17	58.6						

Progressive form of MS(PP,SP) were having significant worse outcome(OR-3.51,95%CI-2.228-7.98,p=0.004) comparing to relapsing MS after analyzing by multiple logistic regression taking other variables like complete recovery after first episode, poly/mono symptomatic, cerebellar, bladder-UMN, MRI-Cerebellar lesion, MRI-brain atrophy, MMF, AZT . Other risk factors were statistically significant in univariate but lose significance with multivariate method. However odd`s ratio and 95% CI signify their prognostic role. Treatment with Mycophenolate was associated with good outcome (OR-0.284,95%CI-0.11-0.683,p=0.051) in univariate analysis. The cyclophosphamide and Mitoxantrone was associated with worse prognosis most probably related to patient selection. The AZT is having no statistically protective role (OR-2.707,95%CI-.622-11.81,p=0.185)

CSF analysis and evoked potential did not predict about worse outcome.

Table-9.1 Outcome analysis of non optico-spinal group (n=69)

Out come	EDSS <6 (n=49)		EDSS ≥6 (n=45)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Male	19	38.8	10	50	1.57	0.55-4.504	.393			
Female(Ref)	30	61.2	10	50						
SP+PP	15	30.6	17	85	12.84	3.26-50.52	.000	2.88	.54-15.36	.214
RR(Ref)	34	69.4	3	15						
Recovery after 1st episode-complete	37	86	7	50	.162	.042-.63	.009			
Presenting symp-Motor	17	34.6	13	65	8.47	.824-87.04	.072			
Presnting symp-Sphincter disturb	1	2	3	15			.037			
Polysymptomatic	11	22.4	14	70	8.06	2.506-25.92	0.000	3.73	.94-14.79	.061
Monosymptomatic(Ref)	38	77.6	6	30						
Cerebellar	19	38.8	14	70	3.684	1.207-11.24	.022	1.36	.29-6.28	.69
U/L ataxia	10	20.4	12	60	5.85	1.88-18.15	.002			
Bladder-UMN	25	51	18	90	8.64	1.807-41.3	.007	3.67	.58-23.17	.166
Bladder- LMN	15	30.6	14	70	5.28	1.703-16.42	.004			
constipation	18	36.7	15	75	5.16	1.608-16.59	.006			

During the presentation the symptoms like visual, sensory, brain stem, cerebellar, does not help in predicting worse out come. The analysis for gender, stroke like, brain stem, hemispheric, myelitis, tumour like, optic neuropathy, Diplopia, Oscillopsia, Nystagmus, INO, ophthalmoplegia, facial myokymia, facial spasm, facial sensory loss, Lhermitte`s, Uhthoff`s, Trigeminal neuralgia, parasthesia , dysesthesia , faecal incontinence, sexual dysfunction, fatigue, vertigo, seizures , no of episodes analysis is not having statistically significant difference as $p>0.05$

Table-9.2 Outcome analysis of non optico-spinal group (n=69)

Out come	EDSS <6 (n=49)		EDSS ≥6 (n=20)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Gait	36	73.5	20	100	6.86	.83-56.5	.073			
Pyramidal	35	71.4	19	95	7.6	.92-62.3	.059			
MRI-cerebellar lesion	12	24.5	10	50	3.083	1.035-9.188	.043			
MRI-basal ganglia lesion	1	2	5	25	16	1.73-147.8	.015			
MRI- cerebral atrophy	20	40.8	18	90	13.05	2.72-62.6	.001			
MMF	36	73.5	12	60	1.113	.28-4.31	.877			
AZT	14	28.6	10	50	2.35	.63-8.73	.22			
First EDSS<6	4	8.2	12	60	7.5	1.92-29.8	.004	1.78	.308-10.29	.518
First EDSS>6(Ref)	45	91.8	8	40						

MS type, poly/mono symptomatic, cerebellar, bladder-UMN, EDSS at first visit were statistically significant in univariate but lose significance with multivariate method. However odd`s ratio and 95% CI signify their prognostic role. Treatment with Mycophenolate is not statistically significant. (OR-1.113, 95%CI-0.28-4.31, p=0.877) in univariate analysis.

Table-10.1 Outcome analysis of optico-spinal group (n=45)

Out come	EDSS <6 (n=36)		EDSS ≥6 (n=9)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Male	14	38.9	4	44.4	1.27	.28-5.49	.76			
Female(Ref)	22	61.1	5	55.6						
SP+PP	8	22.2	8	88.9	28	3.03-258.4	.003	12.75	.76-213.2	.076
RR(Ref)	28	77.8	1	11.1						
Recovery after 1st episode-complete	37	86	7	50	.162	.042-.63	.009			
Polysymptomatic	5	13.9	2	22.2	1.77	.28-11.08	.541			
Monosymptomatic(Ref)	31	86.1	7	77.8						
Cerebellar	11	30.6	3	33.1	1.13	.24-5.39	.872			
Bladder-UMN	23	63.9	6	66.7	1.13	0.24-5.29	.876			
Bladder- LMN	15	41.7	6	66.7	2.8	.603-13.01	.189			
constipation	14	38.9	6	66.7	3.14	.674-14.6	.145			
Urge incontinence	1	2.8	2	22.2	10	.793-126	.075			
Sexual dysfunction	3	8.3	2	22.2	3.143	.44-22.4	.254			
Cerebellar	8	22.2	3	33.3	1.750	.35-8.6	.49			

Because of less number of patients in OSMS group, only 4 variables were analyzed in multivariate model. MS type, MRI- cerebral atrophy, MMF, EDSS at first visit were statistically significant in univariate but lose significance with multivariate method. However odd`s ratio and 95% CI signify their prognostic role.

Table-10.2 Outcome analysis of optico-spinal group (n=45)

Out come	EDSS <6 (n=36)		EDSS ≥6 (n=9)		Unadjusted			Adjusted		
	No	%	No	%	OR	95%CI	p	OR	95%CI	p
Cerebral atrophy	14	38.9	7	77.8	5.5	.99-30.36	.05	1.3	.119-14.2	.829
MMF	27	75	1	11.1	.04	.005-.38	.005	.15	.013-1.95	.15
AZT	10	27.8	4	44.4	.481	.107-2.16	.34			
First EDSs >6	35	97.2	5	55.6	28	2.58-303.5	.006	8.32	.41-168.6	.167
First EDSS <6	1	2.8	4	44.4						

Treatment with Mycophenolate is statistically significant. (OR-0.005,95%CI-0.005-0.38, p=0..005) in univariate analysis. It signify better role of MMF in OSMS than NOSMS.

DISCUSSION

The prevalence of MS in India is approximately 1.33/100,000 as reported by Singhal [9] in the mid eighties from the west coast of India. Study from the France suggested the estimated prevalence was 188.2 cases per 100,000 inhabitants (95% CI: 182.7; 193.8), and the estimated annual incidence was 8.5 cases per 100,000 inhabitants (95% CI: 7.3; 9.7).[106] Over the last one decade, Indian hospital-based studies have shown that, the total proportion of MS-related neurology department admissions increased from 1.58% to 2.54%.[7] Our study depicts MS admission rate as 1.02%. Geographically north west India (above 15◦ N latitude) has 4.15 new cases of MS per year as compared to 3.2 cases per year from south India (below 15◦ N latitude).[107] Previously the diagnosis of multiple sclerosis was based on clinical, electrophysiology, CSF analysis but recently neuroimaging has utmost role. We have selected our cases based on recent McDonald`s criteria.[68]

In the present study the age of onset was 29.38 (±10.09) which is comparable to other Indian studies.[5,108] The youngest and oldest case reported in the present study were 8 and 58 years old respectively. The mean age in PPMS group is 33.38 ±8.18 years which is higher comparing to other groups and also recognized in other studies.[109] Eleven (7%) were children below the age of 16 years at the time of inclusion in the study which is in accordance with previous studies.[110,111]

The female to male ratio was 1.21, which is in agreement with the other studies reported from India.[6,7] Some of the previous Indian studies reported also a higher male ratio. (4, 10) Increase in literary awareness of medical illnesses in our country is probably responsible for

more females being diagnosed as MS. The annualized relapse rate (ARR) is 0.35 /yr which are comparable to the results found in previous studies. [112,113]

In this study, motor weakness was the commonest initial symptom (45.8%) followed by visual impairment (26.7%) and sensory parasthesia (24.2%). These features correlate well with other studies from India[108,114] which documented weakness as the commonest initial presentation similar to western pattern.[59] Though MS in India is not different from the western variety,[108] an increased frequency of visual involvement is a common feature in Asian variety. [3,115] Other Indian studies depict visual symptoms as predominant presenting complaint.[3,6,116] Visual impairment in Japanese and ataxia in western reports were relatively more commoner than Indian series.

These subtle but important differences between different geographical regions within the same country suggest that genetic and environmental factors play an important role in the manifestation of MS. The series from different parts of the country (mostly cross sectional) did not use a common protocol which may account for variation.

Our study showed Pyramidal (86.6%), sensory (68.2%) and bowel and bladder (66.2%) involvement predominate the symptoms/signs observed during the course of illness whereas optic nerve involvement was seen in 58.6% cases.

A major difference in Caucasians and Oriental series has been the incidence of cerebellar involvement which was found in over 80% in the former[117,118] and 30-58% in the latter[5,10,108,119]. In the present study, cerebellar involvement was 36.9 %.

Seizures are uncommon presentation of MS and were noted in nine patients (5.7%) in the present series which was in accordance to the literature with 2.3-5%.[6,120–122] Internuclear ophthalmoplegia (INO) was seen in 9 cases (5.7%) in the present series which was also observed in 6.66% patients in the Gangopadhyay series.[6]

CSF analysis showed mild abnormality (cells>10, Protein>45mg %) in 44 .5% of patients. There was no significant co-relation between severity of abnormality in the CSF and final outcome as measured by EDSS at final visit.

Table No-11 Overview of common features of clinical observational follow –up case series of MS compared with our study.

Author/Reference No.	Jain[12][3]	Sayal[7]	Mani[124]	Gangopadhyay[6]	Bansil[10]	Sarma G R K[116]	Kalanie[109]	Renouxl[125]	Our study
Year covered by study	1957-1980	1986-1998	1991-1996	1989-1999	1990s	1987-1997	1996-2001	1976-2001	2000-2012
Population	Indian	Indian	Indian	Indian	Indian	Indian	Iranian	Europe	Indian
No of Patients	354	100	31	45	81	68	200	684	157
Mean age of onset(years)	27	28.5	25.3	30.5	27.5	26.3	27	13.7±2.4	29.3
Male:Female	1:1.32	1:1.32	1:2.10	1:1.50	1:2.25	1:2.1	1:2.50	1:2.78	1:1.18
Optico-spinal presentation (%)	22-58	47	23	33	NA	25-36	20	NA	37.6
Follow up in yrs	NA	NA	NA	NA	NA	0.5-10	NA	25	1-33
Initial Neurological Symp(%)	NA	Pyramidal inv(46.4)	Visual loss(47)	Visual loss(53.3)	NA	Visual loss(44.1)	Pyramidal	Visual loss(23.4)	Pyramidal(45.8)
Most common Sign during follow up	NA	Pyramidal(87)	Visual impairment(77)	Pyramidal(93.3)	NA	Visual pathway(44.1%)	NA	NA	Pyramidal(86.6)

NA- data not available

Multimodal evoked potentials were done in to look for subclinical anatomical affected sites of demyelination. In our series VEP showed 59.3 %(B/L),18.6% (U/L)abnormality. Other EPs with abnormalities were 67.3%, 51.1% and 39.1% in tibial SSEPs, median SSEPs. BAEP respectively. These evoked potential analysis were similar to previous studies.[73] Thus, Evoked potential studies did not predict worse outcome.

All the patients' had abnormalities in the MRI of the brain and in 85.3% (134/157) abnormalities were detected in the spinal cord imaging. The most common locations were periventricular (95.5%), juxtacortical (93.6%), infratentorial (65.6%) and spinal cord (85.3%). The high frequency of MRI abnormalities were because of strict adherence to recent McDonald`s criteria.[68] The cerebral atrophy was noted more in the EDSS group >6 (86.2% c/w41.2%, p=0.000). The lesion load has not significant correlation with outcome analysis. Previous studies showed brain atrophy had a stronger association with physical disability than T1 hypointense(black hole) and T2 hyperintense lesion load.[126,127].Gado enhancing lesions were noted in 48(30.6%) patient, but did not predict worse outcome. A Meta-analysis study demonstrated that Gado enhancement predicts the occurrence of relapses, but it is not a strong predictor of the development of cumulative impairment or disability.[128] The cerebellar and basal ganglia lesion were associated with worse outcome.

37.6 %(59/157) of the study group had optico-spinal presentation. There is literature on high frequency of optic and spinal cord involvement in several Indian studies[122] and Japan studies.[4] Optico-spinal MS, with attacks restricted clinically to spinal cord and optic nerve were seen in 20-60% of cases.[129] Pandit et al [130] found 47% of their MS cases to have clinical attacks confined to the optic nerve and spinal cord. A paper by Jain et al [123] has been widely

quoted in western literature as evidence for high prevalence of NMO in India. With the recent Wingerchuk criteria[105] for NMO and testing facility for NMO antibody, more number of patients in the OSMS could be diagnosed to have NMO. With this background, in our study, we have taken the optico-spinal group separate from the nonoptico-spinal presentation. Since, we have been doing NMO antibody in the last 3-4 years; we classified the total group as Opticospinal MS (OSMS) and nonoptico-spinal MS (NOSMS) for final outcome analysis. This is corroborated by treatment response to MMF, with the OSMS group having a better outcome.

A number of clinical factors were analyzed, with respect to their validity in assessing the long-term prognosis. In our study the course of the disease was dependent on the onset characteristics, with primary progressive patients experiencing a much more severe course. In patients with an acute onset and complete recovery from first attack were significantly associated with a favorable long-term prognosis. Weinshenker et al has described that women, young age at onset, and without motor onset symptoms were more likely to be considered benign.[131] The factors negatively influencing the prognosis were male sex, age at onset over 25, pyramidal involvement ,more functional systems affected at onset or after 5 years and incomplete first remission.[132] In our study the polysymptomatic presentation, motor, pyramidal involvement and sphincter symptoms at onset had poor outcome. The bowel- bladder symptoms, sexual dysfunction, Cerebellar dysfunction were having worse prognosis looking at the natural history of the disease , similar to other studies.[43,133]

The relapse rate in our study was 3±.36, which did not correlate with outcome, as demonstrated earlier.[134]

Two Indian studies have narrated experience of beta interferon[11] and Mitoxantrone[12] recently. Standard of care provided in our study was IV methylprednisolone for acute attacks and relapses and the DMD's used were AZT (43.3%) and of recently, MMF (54.1%). MMF was associated with significant better outcome in patients in our study (O.R-0.284(C.I-0.11-0.683) p=0.0051. in univariate analysis. Preliminary studies have shown good tolerability and safety when MMF is utilized as monotherapy or in combination with INF or GA.[85,86]

In our study the EDSS of patients at presentation was 4.4±1.31 and at final follow up after 6.16±6.29 years is 4.1±2.31. The median EDSS score was 2.1 in Iran at 5.5years[109] and 3.7 in Gangopadhyay et al series after 6 years post onset[6]. In our study benign MS (EDSS≤6) are 29(18.5%). Earlier Literature suggests that progression of disability in patients with MS is slow[42,49–53] contrary to the some studies.[54] The British Columbia study[52] showed the median time from disease onset to EDSS 6 was 27.9 years and the median age from birth to EDSS 6 was 59 years. So, epidemiological study on a long term basis is required for proper analysis of disability progression. The limitations of the study were Retrospective nature, short duration of follow up and small number of patient. Survival analysis (Kaplan Meir) could not be done for statistical outcome in view of retrospective nature of this study.

In future long term prospective study is suggested for proper analysis of natural history of multiple sclerosis. It would be appropriate to have future trials with DMDs like Mycophenolate and to have a head to head comparison with interferon beta and Glatiramer acetate. This would be of relevance in the developing world resource crunch setting, where health insurance is not available to most of the population and hence treatment is out of pocket payment.

The present study highlights the regional and racial variations in the clinical, imaging and laboratory profile of multiple sclerosis. In our group of patients the salient findings were high incidence of optico-spinal presentation, predominance of relapsing remitting form and low yield of CSF studies. A notable feature is the analysis of prognostic markers of disability progression. The predictors of outcome is about combination of initial demographic and clinical finding with measures of early disease activity and course evaluated clinically along with imaging can be used to predict outcome. There is a definite need for a good marker for disease activity, help decide form of DMDs and predict response to treatment outcome.

Future Directions- There is a need for epidemiological study to look at the disease prevalence and incidence. It is important to interpret the Opticospinal MS which has been reported to be the Asian MS, in the light of Modified Wingerchauk criteria(2006)[105] and NMO antibody. There is a definite need to ideally do randomized double blind control trials comparing the DMDs like Mycophenolate with IFN/ Glatiramer acetate in the developing world setting. Open label studies using Mycophenolate need to be done, if there are ethical issues regarding withhold of standard FDA approved DMDs.

CONCLUSION

- Over a study period of 12 years, there were 157 patients with female preponderance. The observed MS types were RR 85(54.1 %), PP 24(5.3 %), SP47 (29.9 %), PR 1(0.6 %). 59(37.6 %) patient has Opticospinal syndrome presentation and rest 98(62.4%) has non Opticospinal syndrome.

- 47(35.6 %) of RRMS patient, during follow up has attained SPMS.

- EDSS of patients at presentation and at final follow up after 6.16±6.29 years was 4.4±1.31 and 4.1±2.31 respectively. . In our study benign MS (EDSS≤6) are 29(18.5%).

- Progressive form of MS (PP, SP) were having significant worse outcome (OR-3.51, 95%CI-2.228-7.98,p=0.004) when compared to RRMS .

- At first presentation the factors: incomplete recovery, polysymptomatic symptoms like motor, sphincter involvement and during the disease course bowel, bladder, cerebellar and pyramidal involvement were predictors of poor outcome.(Univariate analysis)

- The age, gender, number of episodes, Optico-spinal presentation were not statistically related to outcome analysis.

- Treatment with Mycophenolate is having good outcome (O.R-0.284(C.I-0.11-0.683) p=0.0051. in univariate analysis. The OSMS group had a better outcome with

Mycophenolate when compared to NonOSMS group, suggesting that this probably represents the NMO spectrum.

- The presence of cerebral atrophy and cerebellar involvement showed positive correlation with disability progression.

- CSF OCB was positive in 36.3%.

- There is a definite need for a good marker for disease activity, help decide form of DMDs and predict response to treatment outcome.

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APPENDIX

Appendix 1

PROFORMA FOR THESIS

Longitudinal Follow up study of patients with Multiple sclerosis: Experience from a Tertiary Care Hospital ---

PATIENT –

Name -

Age /Sex -

Address -

H.NO -

DOA -

Types: Relapsing-remitting

Primary-progressive

Secondary-progressive

Progressive-relapsing

Clinical Details of Relapse -

Acute/Sub acute/

Preceding fever -Yes/No

Preceding vaccination –Yes/No

Clinical Features:

Sensory in limbs

Sensory in face

Motor (sub acute)

Motor (acute)

Co-ordination: Gait disturbance/ Limb ataxia/Slurred Speech/Tremor

Vertigo

Visual disturbances: Visual loss/ Diplopia/Oscillopsia/Nystagmus/ Internuclear ophthalmoplegia

Pain: Lhermitte's sign /Trigeminal Neuralgia/ Dysesthetic pain/Visceral pain/Painful tonic spasms

Bladder problems: Urgency/ Incontinence/ Others

Bowel: Constipation/ Incontinence

Sexual Dysfunction

Fatigue

Uhthoff's phenomenon

Seizures

Higher Functions: Attention span / concentration / recent memory / Abstract Conceptualization / Speed of information processing / dementia

Psychiatric disorder: manic depression, paranoia, major depression

Paroxysmal symptoms:

Facial myokymia

Hemi facial spasm

Others

Past Illness/Co-morbidities:

Other Autoimmune disease:

Recent Vaccinations/Viral infections

Sun Exposures

Smoking

Psychosocial Stress:

Month of birth:

Presentation – Monosymptomatic / Polysymptomatic onset

Stroke like

Brainstem-

Cerebellar –

Hemispheric -

Encephalitic -

Myelitis -

Tumour like –

SITE OF NEURAXIS

Optic Neuritis –

Spinal

Hemispheric

Ataxia

Course of disease -

Relapses- Number, Change in disability status

R-R

S-P

PP

PR

Functional Systems:

- pyramidal
- cerebellar
- brainstem
- sensory
- bowel and bladder
- visual
- cerebral
- other

Total number of Episodes- ……..

DISABILITY SCORE

EDSS at presentation -

EDSS at Discharge -

EDSS at final follow up –

Duration of last follow up -

CSF CHARACTERISTICS

Cells: TWBC : L : N: RBCS:

Proteins:

Sugars:

OCBs :

Others :

IMAGING CHARACTERISTICS

At Presentation

Total Lesions(Brain + cord) -

Solitary -

Unilateral -

Bilateral -

Multiple -

Size > 3 cm -

Subcortical –

Deep cortical -

Periventicular -

Corpus Callosum –

Centrum semiovale-

Middle Cerebellar Peduncle -

Brainstem -

Basal Ganglia -

Thalamus -

Gado enhancement – yes/no / not done /

Pattern of enhancement –

Brain Atrophy:

Spinal cord

Spinal cord swelling- Yes/No

Size:

Part of cord involvement:

Cervical + dorsal cord -

> 3 segment –

Gado. Enhancement – yes / no / not given

Last Imaging -

No follow up Imaging -

Total Lesions (Brain + cord) -

Solitary -

Unilateral -

Bilateral -

Multiple -

Size > 3 cm -

Subcortical –

Deep cortical -

Periventicular -

Corpus Callosum –

Centrum semiovale-

Middle Cerebellar Peduncle -

Brainstem -

Basal Ganglia -

Thalamus -

Gado enhancement – yes/no / not done /

Pattern of enhancement –

Spinal cord

Spinal cord swelling- Yes/No

Size:

Part of cord involvement:

Cervical + dorsal cord -

>3 segment -

> 3 segment –

Gado. Enhancement – yes / no / not given

No. of New lesions –

Site of new lesions –

Complete Resolution –

Partial Resolution –

Worsening –

MULTIMODAL EVOKED POTENTIALS

VEPs - Normal Not done Abnormal unilaterally Abnormal Bilaterally

BAER- Normal Not done abnormal

SSEPs –

Median -- Normal Not done Abnormal

Tibial -- Normal Not done Abnormal

TREATMENT DETAILS

ACUTE –

IVIg -

Methylprednisolone -

MPS + IVIg –

Alternative forms of treatment

No treatment -

MAINTANANCE –

Tab.Azathioprine -

Tab.Mycophenolate -

Inj.Cyclophosphamide pulse doses –

Alternate forms of treatment

No Treatment -

Others -

Appendix 2

PATIENT'S INFORMATION AND INFORMED CONSENT

I understand that the department of Neurological sciences is doing a study:

To study the Clinical Profile, Imaging, Electrophysiological and CSF characteristics with special reference to outcome in a cohort of patients diagnosed to have Multiple Sclerosis in the Department of Neurology at CMC, Vellore, during a period of 12 years (2000-2012). The study involves collection of patient information, clinical data and test reports done as part of regular clinical care.

I understand that my withdrawal from the study, at any time will not affect the treatment being given.

Study Title: Natural history of multiple sclerosis in Indian prospective: Experience from a tertiary care hospital.

Study Number:

Subject's Initials: _____ Subject's Name: _____ Date of Birth / Age:_____

Please initial box

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission

to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Sl. No	Hosp No	age	Age@onset	Gender	MS Type	Pre_time	PS_visual	PS_Motor	PS_sensory	PS_BG_Cer	PS_sphinc	Presentation	Brain stem	Cerebellar
1	398205C	17	8	1	1	2	3	2	2	2	2	1	2	2
2	627718C	56	36	2	2	3	3	2	2	2	1	2	2	2
3	050428B	60	35	1	1	2	3	1	2	2	2	1	2	2
4	474298D	34	26	2	1	2	3	5	2	2	2	1	2	1
5	724895D	27	25	1	1	1	3	6	1	2	2	1	2	2
6	728606A	53	38	2	1	1	3	1	2	2	2	1	2	2
7	773085D	32	26	2	3	4	1	6	2	2	2	1	2	1
8	755312D	30	24	2	3	5	2	2	1	2	2	2	1	1
9	976243D	52	44	1	3	5	3	6	2	1	2	1	2	2
10	897142D	24	21	2	1	1	3	6	2	2	2	1	2	2
11	066691F	41	39	2	1	4	3	6	1	2	2	1	2	1
12	371542C	39	30	2	1	1	2	6	2	2	2	1	2	2
13	269167D	47	40	2	1	4	3	6	1	2	2	1	2	1
14	281535D	41	33	1	3	5	3	2	2	1	2	2	1	1
15	076251F	38	34	1	3	5	2	2	2	1	2	2	1	1
16	325909C	39	24	1	2	3	3	4	2	1	2	2	2	2
17	755804D	23	21	1	2	3	3	2	1	1	2	2	2	2
18	191049D	25	20	2	1	4	3	6	2	1	2	1	1	1
19	498108D	23	14	2	3	5	3	1	2	2	2	1	2	2
20	449583D	48	43	1	1	4	3	2	2	2	2	1	2	2
21	885656A	70	46	1	1	4	1	6	2	2	2	1	2	1
22	878454B	37	24	1	3	5	3	6	2	1	2	2	1	1
23	100610F	16	14	1	1	1	3	6	1	2	2	1	2	2
24	735461B	53	38	2	4	6	3	2	2	1	2	2	1	1
25	943384B	32	18	2	3	5	3	2	1	2	2	2	2	2
26	641653D	20	18	1	1	4	2	6	2	2	2	1	2	2
27	460277D	53	50	2	1	1	3	6	2	1	2	1	2	1
28	461869D	49	31	2	3	5	1	6	2	2	2	1	2	1
29	384846D	23	13	1	3	5	3	1	2	2	2	1	2	1
30	418640C	27	15	2	3	5	3	6	1	2	2	1	2	2
31	966226C	55	48	2	1	4	3	6	1	2	2	1	1	1
32	441700D	53	33	1	3	5	1	2	2	1	2	2	1	1
33	466752C	35	26	1	3	4	3	6	2	1	2	1	1	1
34	394227C	60	52	2	1	1	3	6	1	1	2	2	1	1
35	187403D	52	44	2	3	7	3	2	1	2	2	2	1	1
36	941900D	46	38	2	1	4	3	6	1	2	2	1	2	2
37	292956D	22	16	2	1	1	1	6	2	2	2	1	2	2
38	597029B	50	36	1	1	2	3	5	1	1	2	2	2	1
39	101154F	28	25	2	1	4	1	6	2	2	2	1	2	2
40	761303A	15	13	2	3	7	3	4	1	2	1	2	1	1

Sl. No	Hosp No	age	Age@onset	Gender	MS Type	Pre_time	PS_visual	PS_Motor	PS_sensory	PS_BG_Cer	PS_sphinc	Presentation	Brain stem	Cerebellar
41	662799A	62	40	2	1	4	3	6	2	1	2	1	1	1
42	965128D	27	16	1	3	5	1	6	2	2	2	1	1	1
43	397878D	44	41	2	1	2	3	6	1	2	2	1	2	2
44	536739D	42	37	1	2	3	3	2	2	1	2	2	2	2
45	950310D	15	13	1	1	1	2	6	2	2	2	1	2	2
46	938523C	40	32	2	3	4	3	6	1	2	2	1	2	2
47	871636D	47	38	1	3	6	3	2	2	2	2	1	1	1
48	977976D	49	26	2	1	1	1	6	2	2	2	1	1	1
49	055444F	22	19	2	1	4	3	1	2	2	2	1	1	1
50	063366F	30	18	2	3	5	1	6	2	2	2	1	2	1
51	989263D	34	33	2	1	1	3	6	1	2	2	1	2	2
52	953216C	34	28	2	1	1	1	6	2	2	2	1	2	2
53	554003C	36	26	2	1	1	1	6	2	2	2	1	2	2
54	490732D	21	18	1	1	4	3	1	2	1	2	2	2	2
55	450675D	49	30	1	1	4	1	1	2	2	2	2	2	2
56	765896D	33	30	1	1	4	3	1	2	1	2	2	2	2
57	792916D	35	31	2	1	4	3	6	1	2	2	1	2	2
58	792677D	22	18	2	1	4	1	6	2	2	2	1	1	2
59	481813D	35	30	1	3	7	1	6	2	2	2	1	2	2
60	468912D	20	12	2	3	1	3	2	2	1	2	2	1	1
61	849471D	26	21	2	1	1	1	6	2	2	2	1	2	2
62	663658B	31	15	2	1	2	3	6	1	2	2	1	2	2
63	732423D	26	21	2	2	3	3	2	2	2	2	1	2	2
64	730679D	40	34	2	1	4	3	6	2	1	2	1	2	1
65	899657D	19	17	2	1	4	3	2	2	2	2	1	2	1
66	916243D	32	25	2	1	7	3	6	2	1	2	1	2	2
67	997494D	22	17	2	3	4	1	6	2	2	2	1	2	2
68	506633D	50	25	2	1	4	3	6	1	2	2	1	2	2
69	746232D	26	21	2	1	4	2	6	2	1	2	2	1	1
70	452498D	31	29	2	1	1	3	6	1	2	2	1	1	2
71	431844C	33	25	2	2	7	3	2	2	1	2	2	1	1
72	589416D	28	22	1	2	3	3	2	1	2	2	2	2	2
73	621833D	25	23	2	1	4	3	6	1	2	2	1	2	2
74	881952C	39	33	1	1	1	1	6	2	2	2	1	1	2
75	562468D	36	33	1	1	1	3	6	2	1	2	1	1	2
76	411960D	39	28	2	3	5	3	6	1	2	2	1	1	1
77	418170D	25	22	2	1	4	3	6	1	2	2	1	2	2
78	522939D	45	39	2	2	3	3	2	1	1	2	2	2	1
79	523191D	22	16	2	1	4	1	6	2	2	2	1	1	1
80	568976D	36	32	2	2	3	3	6	2	1	2	1	1	1

Sl. No	Hosp No	age	Age@onset	Gender	MS Type	Pre_time	PS_visual	PS_Motor	PS_sensory	PS_BG_Cer	PS_sphinc	Presentation	Brain stem	Cerebellar
81	503082D	42	38	2	1	7	3	6	2	1	2	1	1	2
82	509141D	33	29	1	1	4	3	2	2	2	2	1	2	2
83	413741C	47	41	2	1	4	3	5	2	1	2	2	1	2
84	916614C	52	35	2	3	7	1	6	2	2	2	1	2	2
85	384846D	23	14	1	3	5	3	1	2	2	2	1	2	2
86	320125D	28	24	2	1	1	3	6	1	2	2	1	2	2
87	261700D	32	23	2	3	5	1	6	2	1	2	2	1	1
88	203824D	26	19	2	1	1	3	6	2	1	2	1	1	1
89	205764D	36	23	1	1	4	1	6	2	2	2	1	2	2
90	076819D	45	39	2	2	3	3	1	2	2	2	1	2	2
91	062854D	35	22	2	3	4	1	6	2	2	2	1	2	2
92	448922C	44	22	1	3	5	3	1	2	2	2	1	2	1
93	708203C	31	20	1	1	4	3	1	2	2	2	1	2	2
94	656678C	32	25	1	1	4	3	5	2	2	2	1	2	2
95	642626C	42	34	1	1	4	3	1	2	2	2	1	2	2
96	635641C	41	34	2	1	4	1	6	2	2	2	1	1	2
97	554003C	36	26	2	1	4	1	6	2	2	2	1	2	2
98	733701C	46	26	1	3	5	1	6	2	2	2	1	2	2
99	735379C	46	34	2	2	3	3	2	2	1	2	2	2	1
100	784483C	31	23	1	1	4	3	6	2	2	1	1	2	2
101	877393C	53	45	1	3	7	3	6	2	1	2	1	1	2
102	749124C	42	35	1	1	4	3	6	1	2	2	1	2	2
103	762669C	31	14	2	3	5	3	2	2	2	2	1	2	2
104	695259D	32	26	1	1	4	3	2	2	1	2	2	2	1
105	030804D	67	58	1	1	4	3	2	2	2	1	2	2	1
106	091146D	41	34	1	2	7	3	5	1	1	2	2	1	1
107	136923D	27	20	2	3	5	3	6	2	1	2	1	2	2
108	214084D	27	23	1	1	1	3	2	1	1	2	2	1	2
109	224989D	44	33	1	3	5	3	6	2	2	1	1	2	2
110	298403D	37	29	2	1	1	1	6	2	2	2	1	2	2
111	669940B	44	40	2	1	4	3	6	1	2	2	1	2	2
112	054219C	35	24	2	1	4	3	2	2	2	2	1	2	2
113	572742D	43	36	1	3	5	3	2	1	2	2	2	2	2
114	223278D	34	19	2	3	5	1	6	2	1	2	2	1	1
115	632098D	33	28	1	3	5	3	6	2	1	2	2	1	1
116	297211C	41	32	1	3	5	3	2	2	2	2	1	2	2
117	332937D	54	49	1	2	3	3	2	2	2	1	2	2	2
118	209903C	45	42	1	1	4	1	6	2	2	2	1	2	2
119	917097B	34	28	1	1	1	3	6	2	1	2	1	1	2
120	246960D	60	44	1	3	7	3	6	1	2	2	1	2	2

Sl. No	Hosp No	age	Age@onset	Gender	MS Type	Pre_time	PS_visual	PS_Motor	PS_sensory	PS_BG_Cer	PS_sphinc	Presentation	Brain stem	Cerebellar
121	943183C	34	26	2	3	5	3	6	1	2	2	1	2	2
122	011525F	35	34	1	1	4	1	6	2	2	2	1	2	2
123	985114A	38	17	1	3	5	3	6	2	2	1	1	2	1
124	290373C	29	16	2	1	4	3	1	2	2	2	1	1	1
125	294271C	39	26	2	1	4	3	1	2	2	2	1	2	2
126	316974C	42	23	2	2	3	3	6	1	2	1	2	2	2
127	340576C	30	17	2	1	4	1	6	2	2	2	1	1	2
128	348050C	37	25	1	2	3	3	2	2	1	2	2	1	1
129	348809C	62	51	2	1	4	1	6	2	2	2	1	2	2
130	357767C	43	34	1	1	4	3	6	2	1	2	1	2	2
131	426229C	54	44	1	2	3	3	5	2	2	2	2	2	2
132	447246C	52	39	2	1	4	3	2	2	1	2	2	2	1
133	328997C	28	19	1	1	4	3	5	2	2	2	1	2	1
134	478490C	37	28	2	1	4	1	6	2	2	2	1	2	2
135	499143C	61	40	1	3	7	3	2	2	1	2	2	2	2
136	490488C	32	20	2	1	4	3	6	2	1	2	1	2	2
137	453146C	60	46	1	2	5	3	2	2	1	1	2	2	2
138	660068C	42	25	2	1	4	1	6	2	2	2	1	2	2
139	732030C	60	48	1	3	5	3	1	1	2	2	2	2	2
140	775066C	47	32	1	3	5	1	6	2	2	2	1	2	2
141	918561C	45	36	1	2	3	3	1	2	2	2	1	2	2
142	327322C	58	45	1	2	3	3	2	2	1	1	2	2	2
143	025532D	63	58	2	1	4	3	4	2	2	2	1	2	2
144	035794D	47	34	1	2	3	3	5	1	2	2	2	2	2
145	500939C	47	36	1	2	3	3	2	2	1	2	2	2	1
146	087137D	41	34	2	1	4	3	6	2	1	2	1	2	2
147	090929D	34	26	1	1	4	3	2	2	2	2	1	2	2
148	115887D	50	40	1	3	5	1	1	2	2	2	2	2	1
149	348210D	40	31	1	3	5	3	6	1	2	2	1	2	1
150	351764D	32	28	1	1	4	1	6	2	2	2	1	1	2
151	411306D	43	36	2	2	3	3	2	2	2	1	2	2	2
152	450423D	23	18	2	3	5	3	2	2	1	2	2	2	1
153	192491C	57	40	1	3	5	3	2	2	2	2	1	2	1
154	010771C	39	26	2	1	4	3	2	2	1	2	2	1	1
155	200679C	45	33	1	2	3	3	2	2	1	1	2	2	1
156	099031C	43	30	2	2	3	3	2	2	1	2	2	2	1
157	099436C	41	28	2	1	4	3	5	2	2	2	1	2	2

Sl. No	Hemispheric	Opticospin	Myelitis	OPTIC_NERVE	DIPLOPIA	NYSTAGMUS	INO	OPTHALM	LHERMITTE	UHTHOFF	TRIGEMINAL_ NA	Dysthesia/parasth
1	2	2	1	2	2	2	2	2	1	2	2	1
2	2	2	1	2	2	2	2	2	1	2	2	1
3	2	2	1	2	2	2	2	2	2	2	2	1
4	1	2	2	2	2	2	2	2	1	2	2	1
5	2	2	1	2	2	2	2	2	2	2	2	1
6	2	1	1	1	2	2	2	2	2	2	2	1
7	2	2	1	1	2	2	2	2	2	2	2	1
8	2	2	1	1	2	1	1	2	2	2	2	1
9	2	1	1	1	1	2	2	2	2	2	2	1
10	2	1	1	1	2	2	2	2	2	2	2	2
11	2	2	1	2	2	2	2	2	2	2	2	1
12	2	1	1	1	2	2	2	2	2	2	1	1
13	2	1	1	1	2	2	2	2	1	2	1	1
14	2	2	1	1	1	2	2	2	1	2	2	1
15	2	2	2	1	2	2	2	2	2	2	2	2
16	2	2	1	2	2	2	2	2	2	2	2	2
17	2	2	1	1	2	2	2	2	1	2	2	1
18	2	1	1	1	2	2	2	2	2	2	2	1
19	2	2	1	2	2	2	2	2	1	2	2	1
20	2	1	1	1	2	2	2	2	2	2	2	1
21	2	1	1	1	2	2	2	2	2	2	2	1
22	2	1	1	1	1	1	2	2	2	2	2	1
23	2	2	2	1	2	2	2	2	1	2	2	2
24	2	2	1	2	2	2	2	2	2	2	2	1
25	2	2	1	2	2	2	2	2	1	2	2	1
26	2	2	2	1	2	2	2	2	2	2	2	1
27	2	2	1	2	2	2	2	2	2	2	2	1
28	2	1	1	1	2	2	2	2	2	2	2	1
29	2	1	1	1	2	2	2	2	2	2	2	1
30	2	1	1	1	1	1	2	2	1	2	2	1
31	1	2	1	1	1	1	1	1	1	2	2	1
32	2	2	1	1	1	1	1	1	2	2	2	1
33	2	2	1	1	1	1	2	2	2	2	2	1
34	2	2	2	1	1	1	1	1	2	2	2	2
35	2	2	1	1	1	1	1	1	1	1	1	1
36	2	2	1	2	2	2	2	2	2	1	2	1
37	2	1	1	1	2	2	2	2	2	2	2	1
38	1	2	2	2	2	2	2	2	2	2	2	1
39	1	2	2	1	2	2	2	2	2	2	2	1
40	2	1	1	1	2	2	2	2	2	2	2	1

Sl. No	Hemispheric	Opticospin	Myelitis	OPTIC_NERVE	DIPLOPIA	NYSTAGMUS	INO	OPTHALM	LHERMITTE	UHTHOFF	TRIGEMINAL_ NA	Dysthesia/parasth
41	2	2	2	2	2	1	2	2	2	2	2	1
42	2	2	1	1	1	1	2	1	2	2	2	2
43	2	1	1	1	1	2	2	2	2	2	2	1
44	2	2	1	2	2	2	2	2	2	2	2	1
45	2	1	1	1	2	2	2	2	2	2	2	1
46	2	2	1	2	2	2	2	2	2	2	2	1
47	2	2	1	1	1	1	1	1	2	2	2	2
48	2	2	2	1	1	2	2	1	2	2	2	1
49	2	1	1	1	2	2	2	2	1	2	2	1
50	2	2	1	1	2	2	2	2	2	2	2	1
51	2	2	1	2	2	2	2	2	2	2	2	1
52	2	2	2	1	2	2	2	2	2	2	2	2
53	2	1	1	1	2	2	2	2	2	2	2	1
54	2	1	1	1	2	2	2	2	2	2	2	2
55	2	2	1	1	2	2	2	2	2	2	2	1
56	2	1	2	1	1	1	2	2	2	2	2	1
57	2	1	1	1	2	2	2	2	1	2	2	1
58	2	1	1	1	2	2	2	2	2	2	2	1
59	2	1	1	1	2	2	2	2	2	2	2	1
60	2	1	1	1	1	1	2	2	2	2	2	2
61	2	2	2	1	2	2	2	2	2	2	2	2
62	2	2	1	2	2	2	2	2	2	2	2	1
63	2	2	1	2	2	2	2	2	2	2	2	1
64	2	1	1	1	1	2	2	2	2	2	2	1
65	2	1	1	1	2	2	2	2	2	2	2	1
66	2	1	1	1	1	2	2	2	2	2	1	1
67	2	1	1	1	2	2	2	2	2	2	2	1
68	2	2	1	2	2	2	2	2	2	2	2	1
69	2	2	1	1	1	2	2	2	2	2	2	1
70	2	2	2	2	1	2	2	2	2	2	1	1
71	2	2	2	2	2	2	2	2	2	2	1	1
72	2	2	1	2	2	2	2	2	2	2	2	1
73	2	2	1	2	2	2	2	2	2	2	2	2
74	2	2	2	1	2	2	2	2	2	2	2	2
75	2	2	2	1	1	2	2	2	2	2	2	2
76	1	2	1	1	1	1	2	2	2	2	2	2
77	2	1	1	1	2	2	2	2	2	2	2	1
78	2	2	1	2	2	2	1	1	2	2	2	1
79	2	2	2	1	1	1	2	2	2	2	2	1
80	2	2	2	2	1	1	2	2	2	2	2	2

Sl. No	Hemispheric	Opticospin	Myelitis	OPTIC_NERVE	DIPLOPIA	NYSTAGMUS	INO	OPTHALM	LHERMITTE	UHTHOFF	TRIGEMINAL_ NA	Dysthesia/parasth
81	2	2	1	2	2	2	2	2	1	2	2	1
82	2	1	1	1	2	2	2	2	2	2	2	1
83	2	2	1	2	2	2	2	2	2	2	2	1
84	2	1	1	1	2	2	1	2	2	2	2	1
85	2	1	1	1	2	2	2	2	2	2	2	1
86	2	1	1	1	2	2	2	2	1	2	2	1
87	2	2	1	1	1	1	2	1	2	2	2	1
88	2	2	2	1	1	1	2	1	2	2	2	2
89	2	2	2	1	2	2	2	2	2	2	2	2
90	2	2	1	2	2	2	2	2	2	2	2	2
91	2	1	1	1	2	2	2	2	2	2	2	2
92	2	2	1	2	2	1	2	2	2	2	2	1
93	2	2	1	2	2	2	2	2	2	2	2	2
94	2	2	1	2	2	2	2	2	1	2	2	1
95	2	1	1	2	1	1	2	2	2	2	2	1
96	2	1	1	1	1	2	2	2	2	2	2	1
97	2	1	1	1	2	2	2	2	2	2	2	2
98	2	1	1	1	2	2	2	2	2	2	2	2
99	2	2	1	1	2	1	2	2	2	2	2	2
100	2	1	1	1	2	2	2	2	1	2	2	2
101	2	1	1	1	1	2	2	2	2	2	2	1
102	2	2	1	2	2	2	2	2	2	2	2	1
103	2	1	1	1	2	2	2	2	1	2	2	1
104	2	1	1	1	1	2	2	2	2	1	2	1
105	2	2	2	2	2	2	2	2	2	2	2	2
106	1	2	2	1	1	2	2	2	2	2	2	1
107	2	1	1	1	1	2	2	2	2	2	2	1
108	2	2	2	2	2	2	2	2	2	2	1	1
109	2	1	1	1	2	1	2	2	2	2	2	2
110	2	1	1	1	2	2	2	2	2	2	1	1
111	2	2	1	2	2	2	2	2	2	2	2	1
112	2	1	1	1	1	2	2	2	2	2	2	1
113	2	2	1	2	2	2	2	2	2	2	2	1
114	2	2	1	1	1	1	2	2	2	2	2	1
115	2	2	1	2	1	1	2	2	2	2	2	2
116	2	2	1	2	2	2	2	2	2	1	2	1
117	1	2	1	2	2	2	2	2	2	2	2	1
118	2	1	1	1	2	2	2	2	1	2	2	1
119	2	2	2	2	2	2	2	2	2	2	2	1
120	2	2	1	2	2	2	2	2	1	2	2	1

Sl. No	Hemispheric	Opticospin	Myelitis	OPTIC_NERVE	DIPLOPIA	NYSTAGMUS	INO	OPTHALM	LHERMITTE	UHTHOFF	TRIGEMINAL_ NA	Dysthesia/parasth
121	2	2	1	2	2	2	2	2	2	2	2	1
122	1	2	2	1	2	2	2	2	2	2	2	1
123	2	1	1	1	2	2	2	2	1	2	2	1
124	2	2	1	1	2	2	2	2	2	2	2	1
125	2	2	1	2	2	2	2	2	2	2	2	1
126	2	2	1	2	2	2	2	2	2	2	2	1
127	2	1	1	1	1	1	2	1	2	2	2	1
128	2	2	1	2	1	1	2	1	2	2	2	2
129	2	1	1	1	2	2	2	2	2	2	2	2
130	2	1	1	1	1	2	2	2	2	2	2	2
131	1	2	2	2	2	2	2	2	2	2	2	2
132	2	2	2	2	2	2	2	2	2	2	2	2
133	1	2	2	2	2	2	2	2	2	2	2	2
134	1	2	1	1	2	2	2	2	2	2	2	2
135	2	2	1	2	2	2	2	2	2	2	2	2
136	2	1	1	1	1	1	2	2	1	2	2	1
137	2	2	1	2	2	2	2	2	2	2	2	2
138	2	1	1	1	2	2	2	2	2	2	2	2
139	2	2	1	2	2	2	2	2	2	2	2	1
140	2	1	1	1	2	2	2	2	2	2	2	1
141	2	2	1	2	2	2	2	2	2	1	2	2
142	2	2	1	2	2	1	2	2	2	2	2	2
143	2	2	1	2	2	2	2	2	2	2	2	1
144	2	2	1	2	2	2	2	2	2	2	2	1
145	2	2	1	2	2	2	2	2	2	2	2	2
146	2	1	1	1	1	1	2	2	2	2	2	2
147	2	2	1	2	2	2	2	2	2	2	2	1
148	2	1	1	1	2	2	2	2	2	2	2	2
149	2	1	1	1	2	1	2	2	2	2	2	2
150	2	1	1	1	1	1	2	2	2	2	2	2
151	2	2	1	2	2	2	2	2	2	2	2	2
152	2	2	1	2	2	2	2	2	2	2	2	2
153	2	2	1	2	2	2	2	2	1	2	2	1
154	2	1	1	1	1	1	2	2	2	2	2	1
155	2	2	1	2	2	1	1	1	2	2	2	2
156	2	2	2	2	2	1	2	2	2	2	2	2
157	1	2	1	2	2	2	2	2	2	2	2	2

Sl. No	B_UMN	LMN	CONSTIPATION	INCONTINENCE	SEXUAL_ DYS	FATIGUE	GAIT_INV	LIMB_ATAXIA	VERTIGO	SEIZURES	Pyramidal	Total Epis	EDSS@Pre
1	2	2	2	2	2	2	1	2	2	1	1	6	6.5
2	1	1	1	2	2	1	1	2	2	2	1	1	8
3	2	2	2	2	2	2	1	2	2	2	1	5	4.5
4	1	2	1	2	2	2	1	1	1	2	1	2	2
5	2	2	2	2	2	2	2	2	2	2	1	2	1
6	2	2	2	2	2	2	1	2	2	2	2	3	4
7	1	1	1	2	2	1	1	2	2	2	1	6	4
8	1	2	1	1	2	1	1	1	2	1	1	4	6.5
9	1	1	1	2	1	1	1	2	2	2	1	4	4
10	2	2	2	2	2	2	1	2	2	2	1	4	2.5
11	1	2	2	2	2	1	2	2	1	2	1	3	2.5
12	2	2	2	2	2	2	1	1	2	2	1	4	7
13	1	1	2	2	2	1	2	2	2	2	1	2	2.5
14	1	1	1	2	1	1	2	1	2	2	1	3	6.5
15	1	2	2	2	1	2	1	1	1	2	2	3	6.5
16	1	2	2	1	1	2	1	2	2	1	1	1	4
17	1	1	1	2	1	2	1	2	2	2	1	1	5
18	1	2	2	2	2	1	1	1	2	2	1	2	5
19	1	1	1	2	2	1	1	2	2	2	1	3	4.5
20	1	2	1	2	2	1	1	2	2	2	1	3	3
21	1	1	1	2	2	2	1	2	2	2	1	4	5.5
22	1	1	1	1	2	1	1	1	2	2	1	4	4
23	2	2	2	2	2	2	2	2	2	2	2	2	1
24	1	1	1	2	2	1	1	1	2	2	1	1	5
25	1	2	1	2	2	2	1	2	2	2	1	3	4
26	2	2	2	2	2	1	2	2	2	2	2	2	3
27	2	2	2	2	2	1	1	2	2	2	2	2	3
28	1	1	2	2	2	1	1	2	2	1	1	3	5
29	1	1	1	2	1	1	1	2	2	2	1	4	5
30	1	1	1	2	2	1	1	2	2	2	1	4	4.5
31	1	1	2	2	2	1	1	1	1	2	1	4	4
32	1	1	1	2	2	1	1	1	1	1	1	3	5
33	1	1	1	2	1	1	1	2	1	2	1	3	4
34	1	2	2	2	2	2	1	2	1	2	2	2	3
35	1	1	1	2	2	1	1	2	1	2	1	3	4
36	2	2	2	2	2	1	1	2	2	2	1	3	1.5
37	2	2	2	2	2	2	2	2	2	2	1	4	2
38	2	2	2	2	2	1	1	1	2	2	1	1	5
39	2	2	2	2	2	2	2	2	1	2	1	2	5
40	1	1	1	2	2	2	1	1	1	2	1	3	7

Sl. No	B_UMN	LMN	CONSTIPATION	INCONTINENCE	SEXUAL_ DYS	FATIGUE	GAIT_INV	LIMB_ATAXIA	VERTIGO	SEIZURES	Pyramidal	Total Epis	EDSS@Pre
41	1	2	1	2	2	1	1	2	1	2	1	3	5
42	1	1	1	2	1	1	1	1	2	2	1	3	6.5
43	1	1	1	2	2	1	1	2	1	2	1	2	3
44	1	1	1	2	1	1	1	2	1	2	1	1	4.5
45	1	1	1	2	2	2	2	2	2	2	1	2	4.5
46	1	1	1	2	2	1	1	2	2	2	1	4	4
47	1	2	1	2	1	2	1	1	1	2	1	3	5
48	2	2	2	2	2	2	2	2	1	2	2	5	2
49	1	1	1	2	2	1	1	1	1	2	1	5	5
50	1	1	1	2	2	2	1	1	1	2	1	4	5
51	1	2	1	2	2	2	2	2	2	2	1	1	2.5
52	2	2	2	2	2	2	2	2	2	2	2	1	2
53	2	2	2	2	2	1	1	2	2	1	1	2	3.5
54	2	2	2	2	1	1	1	2	2	2	1	3	2.5
55	1	1	1	2	2	1	1	2	2	2	1	4	4.5
56	1	2	2	2	2	2	1	1	1	2	1	3	5.5
57	1	2	2	2	2	1	1	1	2	2	1	3	3
58	2	2	2	2	2	1	2	2	1	2	1	3	3
59	1	1	1	2	1	1	1	2	2	2	1	2	6
60	2	2	2	2	2	1	1	1	2	2	1	3	4.5
61	2	2	2	2	2	1	2	2	1	2	2	3	2.5
62	2	2	2	2	2	2	1	2	2	2	2	9	4
63	1	2	2	2	2	2	1	2	2	2	1	1	5
64	1	2	2	2	2	1	1	1	2	1	1	3	5
65	1	2	2	2	2	1	1	2	2	2	1	2	4.5
66	2	2	2	2	2	2	1	2	2	2	1	6	3
67	1	2	1	1	2	1	1	2	2	2	1	4	5.5
68	2	2	2	2	2	2	1	2	2	2	1	2	3.5
69	2	2	2	2	2	2	1	1	1	2	1	4	4.5
70	2	2	2	2	2	2	2	2	2	2	2	2	2.5
71	1	2	1	2	2	1	1	1	1	2	1	1	5
72	2	1	2	2	2	1	1	2	2	2	1	1	4.5
73	1	1	2	2	2	1	1	2	2	2	1	2	4.5
74	2	2	2	2	2	2	2	2	2	2	2	2	2.5
75	2	2	2	2	2	2	2	2	2	2	2	1	2
76	1	1	1	2	2	1	1	1	2	2	1	5	6
77	1	1	1	2	2	1	1	2	2	2	2	2	3.5
78	1	1	1	2	2	1	1	1	2	2	1	1	6
79	1	2	2	2	2	1	1	2	1	2	2	3	4
80	2	2	2	2	2	1	1	1	2	2	2	1	4.5

Sl. No	B_UMN	LMN	CONSTIPATION	INCONTINENCE	SEXUAL_ DYS	FATIGUE	GAIT_INV	LIMB_ATAXIA	VERTIGO	SEIZURES	Pyramidal	Total Epis	EDSS@Pre
81	1	1	1	2	2	1	1	2	1	2	1	3	4
82	1	1	1	2	2	1	1	2	2	2	1	3	4.5
83	1	1	1	2	2	1	1	2	1	2	1	3	4.5
84	1	2	2	2	2	1	1	2	2	2	1	5	5
85	1	1	1	2	2	1	1	2	2	2	1	4	4
86	1	2	2	2	2	1	1	2	2	2	1	3	3
87	1	1	2	2	2	1	1	1	2	2	1	4	6.5
88	2	2	2	2	2	1	2	2	1	2	1	2	4
89	1	2	2	2	2	2	1	2	2	2	1	3	4.5
90	1	2	2	2	2	2	1	2	2	2	1	1	5
91	1	1	1	2	2	1	1	2	2	2	1	2	4
92	2	2	2	2	2	1	1	1	2	2	1	5	4
93	1	1	1	2	1	1	1	2	2	2	1	4	5
94	2	2	2	2	2	1	1	2	2	2	1	2	4
95	1	1	1	2	2	1	1	2	2	2	1	3	6
96	1	2	2	2	2	1	1	2	2	2	1	4	5
97	1	2	2	2	2	2	1	2	2	2	1	2	5
98	1	1	1	1	2	1	1	2	2	2	1	5	5
99	2	2	2	2	2	1	1	1	2	2	1	1	4.5
100	1	1	1	2	1	1	1	2	2	2	1	5	5
101	1	1	1	2	2	1	1	2	2	2	1	3	3
102	2	2	2	2	2	1	1	2	2	2	1	3	4
103	1	1	1	1	2	1	1	2	2	2	1	5	5
104	2	2	2	2	2	1	1	1	1	2	1	4	4
105	1	1	1	1	2	1	1	1	2	2	1	3	5
106	2	2	2	2	2	2	1	1	2	2	1	1	5
107	1	1	1	1	2	1	1	2	1	2	1	3	6
108	2	2	2	2	2	1	1	2	1	2	1	2	3.5
109	1	1	2	2	2	1	1	2	2	2	1	3	4
110	2	2	2	2	2	2	2	2	1	2	1	4	3.5
111	2	2	2	2	2	1	1	2	2	2	1	2	4
112	1	1	1	2	2	1	1	2	2	2	1	3	6
113	1	1	1	2	1	2	1	2	2	2	1	2	8
114	1	1	1	2	2	1	1	1	1	2	1	5	6
115	1	2	1	2	1	1	1	1	2	2	1	3	4
116	1	1	1	2	1	1	1	2	2	2	1	3	4
117	1	2	1	2	1	1	1	2	2	2	1	1	4.5
118	2	2	2	2	2	2	2	2	2	2	1	3	3
119	2	2	2	2	2	1	1	2	2	2	1	2	3.5
120	2	2	1	2	1	1	1	2	2	2	1	2	8

Sl. No	B_UMN	LMN	CONSTIPATION	INCONTINENCE	SEXUAL_ DYS	FATIGUE	GAIT_INV	LIMB_ATAXIA	VERTIGO	SEIZURES	Pyramidal	Total Epis	EDSS@Pre
121	1	1	1	2	2	1	1	2	2	2	1	5	5
122	2	2	2	2	2	1	1	2	2	2	1	2	4
123	1	2	2	2	1	1	1	1	2	2	2	7	6
124	2	2	2	2	2	2	1	1	1	2	1	4	4.5
125	1	1	1	1	2	1	1	2	2	2	1	1	7
126	1	1	1	1	2	1	1	2	2	2	1	1	6.5
127	1	1	2	2	2	1	1	2	1	2	1	4	5
128	2	2	2	2	2	1	1	1	1	1	1	1	6
129	2	2	2	2	2	1	1	2	2	2	1	3	4
130	2	2	2	2	2	2	1	2	2	2	1	2	4
131	2	2	1	2	2	2	1	2	2	2	1	1	4.5
132	2	2	2	2	2	2	1	1	2	2	1	12	4
133	2	2	2	2	2	2	1	1	2	2	1	3	4.5
134	2	2	2	2	2	2	2	2	2	2	1	3	3
135	1	1	1	2	2	1	1	2	2	1	1	3	6.5
136	1	1	1	2	2	1	1	2	2	2	1	2	4
137	1	1	1	2	2	2	1	2	2	2	1	1	4.5
138	2	2	2	2	2	2	1	2	2	2	1	3	4
139	2	2	2	2	2	2	1	2	2	2	1	2	4.5
140	1	1	1	1	2	2	1	2	2	2	1	3	5
141	2	2	2	2	2	2	1	2	2	2	1	1	4
142	1	1	1	2	1	1	1	2	2	2	1	1	5
143	1	1	1	2	2	2	1	2	2	2	2	3	8
144	2	2	2	2	2	2	1	2	2	2	1	1	4.5
145	1	1	1	1	1	1	1	1	2	2	1	1	5.5
146	1	1	1	2	2	1	1	2	2	2	1	3	4.5
147	1	2	2	2	2	1	1	2	2	2	1	3	4
148	2	1	1	2	1	1	1	1	2	2	1	5	4.5
149	2	2	2	2	2	1	1	1	2	2	1	3	6
150	2	2	2	2	2	2	1	2	2	2	1	5	4
151	1	1	1	2	2	1	1	2	2	2	1	1	4.5
152	1	1	1	2	2	2	1	1	2	2	1	3	4
153	1	1	1	2	2	1	1	2	2	2	1	3	4.5
154	1	1	2	2	2	2	1	1	2	2	2	4	4.5
155	1	1	1	2	1	1	1	1	2	2	1	2	4.5
156	1	2	2	2	2	1	1	1	2	2	2	1	5
157	2	2	2	2	2	2	1	2	2	2	2	2	4.5

Sl. No	EDSS@Pres	CSF_PROTEIN	CSF_PROTEIN	CELLS	OCB	VEP	BAEP	SSEP_MEDIAN	SSEP_TIBIAL	MRI_LESIONS	JUXTRACORTICAL	PERIVENTRICULAR	Sl. No
1	2.5	2	1	1	2	1	1	1	1	2	2	1	1
2	7	4	1	1	2	3	1	1	2	4	1	1	2
3	1	1	1	2	3	1	1	2	2	4	1	1	3
4	2	1	1	1	1	1	3	3	1	4	1	1	4
5	1	1	1	1	1	2	3	1	1	4	1	1	5
6	1	1	1	2	2	5	5	5	5	4	1	1	6
7	4.5	3	1	1	2	3	1	2	2	4	1	1	7
8	5.5	3	1	2	2	3	3	2	2	4	1	1	8
9	4	2	2	1	2	2	3	3	2	4	1	1	9
10	1.5	1	2	3	1	3	1	2	2	4	1	1	10
11	2.5	2	1	2	1	1	3	1	2	2	2	1	11
12	2.5	2	2	1	2	1	3	1	1	1	2	1	12
13	2.5	2	2	1	2	1	3	1	1	2	2	1	13
14	7	4	2	1	3	1	3	3	1	4	2	2	14
15	7	4	1	1	2	3	3	3	2	4	1	1	15
16		6	2	1	1	3	1	3	3	4	1	1	16
17	4	2	2	1	1	3	3	3	1	4	1	1	17
18	1	1	1	1	2	3	2	3	2	4	1	1	18
19	3.5	2	1	1	1	1	3	3	2	4	2	1	19
20	2.5	2	2	1	2	3	3	3	2	2	1	1	20
21	4	2	1	1	3	2	1	2	2	2	1	1	21
22	5.5	3	2	3	3	3	3	3	3	4	1	1	22
23	1	1	1	2	2	3	1	1	1	2	1	1	23
24	8	4	1	1	2	3	1	2	2	4	1	1	24
25	3	2	1	1	3	1	2	2	2	4	1	1	25
26	1	1	1	3	1	3	1	1	2	4	1	1	26
27	1	1	2	1	2	3	3	3	2	4	1	1	27
28	4	2	2	1	2	3	3	3	2	4	1	1	28
29	3	2	1	1	2	3	3	3	2	4	1	1	29
30	8	4	1	1	1	3	2	2	2	4	1	1	30
31	3	2	1	1	2	3	2	3	2	4	1	1	31
32	5	3	2	1	2	3	2	1	2	4	1	1	32
33	4.5	3	2	1	2	3	2	3	2	4	1	1	33
34	2.5	2	1	1	2	2	1	1	1	4	1	1	34
35	6.5	4	1	1	2	1	3	1	2	4	2	2	35
36	1.5	1	2	2	2	1	3	1	2	4	1	1	36
37	1	1	1	3	1	3	3	1	1	4	1	1	37
38	2	1	2	1	3	3	1	3	1	1	2	2	38
39	4	2	1	1	2	2	3	2	2	1	1	2	39
40	10	5	1	1	3	3	3	2	2	4	1	1	40

Sl. No	EDSS@Pres	CSF_PROTEIN	CSF_PROTEIN	CELLS	OCB	VEP	BAEP	SSEP_MEDIAN	SSEP_TIBIAL	MRI_LESIONS	JUXTRACORTICAL	PERIVENTRICULAR	Sl. No
41	3	2	2	1	2	1	1	1	1	4	1	1	41
42	6.5	4	1	3	2	3	3	2	2	4	1	1	42
43	2.5	2	1	1	1	1	1	3	1	4	1	1	43
44	5.5	3	1	1	3	1	3	2	2	4	1	1	44
45	3	2	1	1	2	3	3	3	2	1	1	2	45
46	6.5	4	1	1	1	3	1	2	2	4	1	1	46
47	6	4	1	2	2	3	3	2	2	4	1	1	47
48	2	1	1	1	1	3	1	1	1	4	1	1	48
49	4	2	2	1	2	3	1	1	2	4	2	2	49
50	4.5	3	2	1	2	3	3	2	2	4	1	1	50
51	2	1	1	1	2	1	3	2	1	4	1	1	51
52	1	1	1	1	2	2	1	1	1	1	1	1	52
53	3	2	1	1	2	2	1	2	2	4	1	1	53
54	2	1	1	1	2	3	3	3	3	4	1	1	54
55	4	2	1	1	1	3	1	2	2	4	1	1	55
56	4	2	2	2	2	3	3	3	2	4	1	1	56
57	3	2	1	1	2	1	3	3	1	1	2	2	57
58	10	5	1	1	1	3	3	1	2	4	1	1	58
59	8	4	2	1	2	1	3	1	2	4	1	1	59
60	3	2	1	1	1	3	2	2	2	4	1	1	60
61	2	1	2	1	1	2	3	1	1	4	1	1	61
62	2	1	1	1	1	3	1	1	2	4	1	1	62
63	5.5	3	1	1	2	2	3	3	2	4	1	1	63
64	3	2	1	1	1	3	1	3	2	4	1	1	64
65	3	2	2	1	2	3	3	2	2	4	1	1	65
66	2.5	2	1	2	2	3	3	3	2	4	1	1	66
67		6	1	1	2	3	3	1	3	4	1	1	67
68	1	1	1	1	2	2	3	1	1	4	1	1	68
69	3	2	1	1	1	3	3	3	3	4	1	1	69
70	2	1	1	2	2	3	3	1	2	4	1	1	70
71		6	1	1	1	1	1	1	1	4	1	1	71
72	5.5	3	2	2	3	3	3	2	2	4	1	1	72
73	3	2	1	2	2	4	3	3	3	4	1	1	73
74	1	1	2	2	2	3	2	2	2	4	1	1	74
75	0	1	1	2	1	2	3	3	1	2	1	1	75
76	5	3	1	1	2	3	3	3	2	4	1	1	76
77	2	1	1	1	2	2	3	3	1	4	1	1	77
78	6.5	4	1	1	2	3	3	2	2	4	1	1	78
79	2.5	2	1	1	2	3	2	1	2	4	1	1	79
80	5	3	1	1	1	3	3	3	1	4	1	1	80

Sl. No	EDSS@Pres	CSF_PROTEIN	CSF_PROTEIN	CELLS	OCB	VEP	BAEP	SSEP_MEDIAN	SSEP_TIBIAL	MRI_LESIONS	JUXTRACORTICAL	PERIVENTRICULAR	Sl. No
81	2.5	2	1	2	2	1	2	1	1	4	1	1	81
82	3	2	2	1	2	3	3	2	2	4	1	1	82
83		6	1	1	2	2	3	2	2	4	1	1	83
84	6.5	4	1	1	1	4	3	3	3	4	1	1	84
85	3	2	1	1	1	3	2	3	2	4	1	1	85
86	2	1	1	1	2	3	3	3	1	4	1	1	86
87	7	4	2	1	1	3	3	2	2	4	1	1	87
88	1	1	2	1	2	2	3	3	2	4	1	1	88
89	4	2	1	1	2	2	3	1	1	4	1	1	89
90		6	2	1	1	3	3	3	2	4	1	1	90
91	5	3	1	1	1	3	1	2	3	4	1	1	91
92	5.5	3	1	1	1	3	1	2	2	4	1	1	92
93	4	2	1	1	1	3	3	2	2	4	1	1	93
94		6	1	2	1	1	1	1	1	2	1	1	94
95		6	2	1	2	3	3	3	3	4	1	1	95
96	4	2	2	2	2	1	1	2	2	4	1	1	96
97		6	1	1	1	2	2	3	2	4	1	1	97
98		6	1	2	1	3	2	2	2	4	1	1	98
99		6	1	1	2	3	2	1	3	4	1	1	99
100		6	1	1	2	2	1	1	1	4	1	1	100
101	4	2	2	2	2	3	3	3	2	3	1	1	101
102		6	1	1	2	1	1	3	1	4	1	1	102
103		6	2	2	1	3	2	1	1	4	1	1	103
104	3	2	1	2	2	3	2	2	2	4	1	1	104
105	7	4	2	1	2	3	2	2	2	4	1	1	105
106	7	4	2	1	2	1	1	1	1	4	1	1	106
107	8	4	1	1	2	3	1	2	1	4	1	1	107
108		6	1	1	2	1	3	1	1	4	1	1	108
109		6	1	1	2	2	3	1	3	4	1	1	109
110	5	3	1	1	1	2	3	2	2	4	1	1	110
111	1	1	1	1	2	1	3	3	2	4	1	1	111
112		6	1	1	1	3	3	3	2	4	1	1	112
113		6	2	1	1	2	3	3	2	4	1	1	113
114	7	4	2	1	2	3	1	2	2	4	1	1	114
115	6	4	1	2	2	1	3	1	2	4	1	1	115
116		6	1	1	2	3	3	1	1	4	1	1	116
117	5.5	3	1	1	2	1	1	3	1	4	1	1	117
118	1	1	1	1	2	3	3	3	1	4	1	1	118
119		6	2	2	1	2	3	3	2	4	1	1	119
120		6	2	1	1	1	1	2	2	4	1	1	120

Sl. No	EDSS@Pres	CSF_PROTEIN	CSF_PROTEIN	CELLS	OCB	VEP	BAEP	SSEP_MEDIAN	SSEP_TIBIAL	MRI_LESIONS	JUXTRACORTICAL	PERIVENTRICULAR	Sl. No
121	7	4	1	1	1	1	2	3	1	4	1	1	121
122	2	1	2	1	2	2	3	1	1	2	1	1	122
123		6	2	1	2	2	3	2	2	4	1	1	123
124		6	1	1	2	2	1	1	2	4	1	1	124
125		6	1	1	2	5	5	5	5	4	1	1	125
126	7	4	1	2	2	3	3	2	2	4	1	1	126
127		6	1	1	1	3	2	3	2	4	1	1	127
128		6	1	1	1	3	2	2	2	4	1	1	128
129		6	1	1	1	2	3	3	2	4	1	1	129
130		6	1	1	1	1	1	1	1	2	1	1	130
131		6	2	1	2	3	1	1	2	4	1	1	131
132		6	1	1	1	2	3	1	2	4	1	1	132
133		6	1	2	1	5	5	5	5	4	1	1	133
134		6	1	1	2	3	3	2	1	4	1	1	134
135		6	1	1	2	3	3	3	3	4	1	1	135
136		6	1	1	1	3	2	2	1	4	1	1	136
137		6	2	1	3	3	3	3	3	4	1	1	137
138	5.5	3	1	1	1	3	1	3	3	4	1	1	138
139		6	2	1	1	3	2	3	2	4	1	1	139
140	8	4	1	2	2	2	1	2	2	4	1	1	140
141		6	1	1	2	5	5	5	5	4	1	1	141
142		6	2	1	2	3	2	2	2	4	1	1	142
143	5	3	1	1	2	1	1	1	1	4	1	1	143
144	6.5	4	1	1	2	1	1	1	2	4	1	1	144
145		6	1	1	1	3	2	2	2	4	1	1	145
146	2	1	1	1	2	2	3	1	1	4	1	1	146
147	7	4	1	2	1	3	2	2	2	4	1	1	147
148	7	4	1	1	1	3	3	2	2	4	1	1	148
149	8.5	5	1	1	1	3	3	3	2	4	1	1	149
150	5	3	1	1	2	1	1	1	1	4	1	1	150
151		6	2	1	2	3	3	3	2	4	1	1	151
152	7	4	1	1	2	3	3	3	2	4	1	1	152
153	8	4	1	1	2	3	3	3	2	4	1	1	153
154		6	1	2	2	3	2	2	2	4	1	1	154
155		6	2	2	3	3	2	3	2	4	1	1	155
156		6	2	3	2	3	3	3	1	4	1	1	156
157		6	1	1	2	5	5	5	5	4	1	1	157

INFRATENTORIAL	CC	DAWSON_F	Ce	BRAIN STEM	BG	THALAMUS	SIZE_LES	GADO	CERVICAL	Cerebral atrophy type	F/U MRI after	Improvement	Atrophy
2	2	2	2	2	2	2	1	1	1	4	8	2	2
2	2	2	2	2	2	2	1	2	1	5	7	3	1
1	2	2	2	2	2	2	1	2	1	2	11	1	1
1	1	2	2	1	2	2	1	2	1	4	3	3	2
1	1	2	1	1	2	2	1	1	1	4	3	1	2
1	1	2	2	1	2	2	1	1	1	4	7	2	2
1	1	2	1	1	2	2	1	2	1	2	3	2	1
1	1	2	1	1	2	2	1	1	1	5	3	3	1
2	1	1	2	2	2	2	1	2	2	2	3	3	1
2	1	2	2	2	2	2	1	1	1	4	2	3	2
1	1	2	2	1	2	2	1	2	2	4	0	0	2
1	2	2	2	1	2	2	1	2	1	4	9	1	2
2	1	2	2	2	2	2	1	2	2	4	2	3	2
1	2	2	1	1	2	2	1	1	1	2	3	1	1
1	2	2	2	1	2	2	1	2	2	2	1	3	1
1	1	2	2	1	2	2	1	2	1	5	1	3	1
1	1	2	2	1	2	2	1	1	1	2	3	2	1
1	1	1	2	1	2	1	1	1	1	4	4	1	2
1	1	1	2	1	2	2	1	1	1	4	0.4	3	2
2	2	2	2	2	2	2	1	2	2	4	0	0	2
1	2	2	2	1	2	2	1	1	2	4	0	0	2
1	1	2	2	1	2	1	1	2	1	4	0	0	2
2	1	1	2	2	2	2	1	1	2	4	0.5	1	2
1	1	1	1	1	1	1	1	1	1	5	9	2	1
2	1	2	2	2	2	2	1	2	1	4	0	0	2
1	1	1	2	1	2	2	1	2	1	4	0.4	3	2
1	1	2	2	1	2	2	1	1	1	4	2	3	2
1	1	2	2	1	2	2	1	2	1	4	1	3	2
2	1	2	2	2	2	2	1	1	1	2	2	3	1
1	1	2	1	1	2	2	1	1	1	4	0.5	1	2
2	1	1	2	2	2	2	1	2	1	4	3	2	2
1	1	2	2	2	2	2	1	2	1	5	2	2	1
1	1	2	1	1	2	2	1	2	1	2	6	2	1
1	2	2	2	1	2	2	1	2	2	4	0	0	2
2	2	2	2	1	2	2	1	1	1	2	2	2	1
2	2	2	2	2	2	2	1	2	1	2	1	2	1
1	1	1	1	1	2	2	1	1	1	4	3	1	2
2	2	2	2	2	2	2	2	1	2	2	5	1	1
2	2	2	2	2	2	1	3	1	1	4	0.5	3	2
1	1	2	2	1	2	2	1	2	1	2	0	0	1

INFRATENTORIAL	CC	DAWSON_F	Ce	BRAIN STEM	BG	THALAMUS	SIZE_LES	GADO	CERVICAL	Cerebral atrophy type	F/U MRI after	Improvement	Atrophy
1	1	2	1	1	2	2	1	1	2	2	2	1	1
1	1	2	1	1	2	2	1	2	1	5	0	0	1
1	1	2	2	1	2	2	1	1	1	4	2	3	2
2	1	2	2	2	2	2	1	2	1	4	2	3	2
2	2	2	2	2	2	2	1	2	2	2	0	0	1
1	1	1	2	2	2	2	1	1	1	2	4	2	1
1	1	2	2	2	2	2	1	2	1	5	1	2	1
1	1	1	2	2	2	2	1	2	1	2	1	1	1
2	2	2	2	1	2	2	1	1	1	2	0.5	2	1
1	1	1	1	1	2	2	1	2	1	5	0	1	1
1	1	1	2	1	2	2	1	1	1	4	0.4	1	2
2	1	2	2	2	2	2	1	1	1	4	6	1	2
2	1	2	2	2	2	2	1	2	1	4	4	3	2
1	1	2	2	1	2	2	1	1	1	4	0	0	2
1	1	2	2	1	2	2	1	2	1	4	1	3	2
1	2	2	1	1	2	2	1	2	2	4	1	1	2
2	2	2	2	2	2	2	1	2	1	4	1	3	2
2	1	1	2	2	2	2	1	2	1	4	0	0	2
2	2	2	2	2	2	2	1	2	1	2	0	0	1
1	2	2	1	1	2	1	1	1	1	2	1	2	1
2	1	2	2	2	2	2	1	1	1	4	1	3	2
1	1	1	2	1	2	2	1	1	1	2	13	2	1
1	1	2	2	1	2	2	1	2	1	4	0	0	2
1	2	2	2	1	2	2	1	2	1	2	0.5	2	1
1	1	1	1	1	2	2	1	1	1	5	1	2	1
2	1	2	2	1	2	2	1	2	1	4	0.3	3	2
1	2	2	2	1	2	2	1	2	1	4	1	2	2
1	1	1	2	1	2	2	1	1	1	4	3	3	2
1	1	1	2	1	2	2	1	1	1	4	0	0	2
1	2	2	1	1	2	2	1	2	1	2	3	2	1
1	1	1	1	1	1	2	1	2	1	2	5	1	1
1	2	2	2	1	2	2	1	2	1	2	3	2	1
1	1	1	2	1	2	2	1	2	1	4	0	0	2
1	1	1	2	1	2	2	1	2	1	2	5	3	1
2	2	2	2	2	2	2	1	2	1	4	0	0	2
1	1	1	1	1	1	1	1	2	1	5	2	2	1
1	1	2	2	1	2	2	1	2	1	2	3	1	1
1	1	1	1	1	2	2	1	2	1	2	1	3	1
1	1	1	2	1	2	2	1	2	1	4	0.5	1	2
1	1	2	2	1	2	2	1	2	1	5	2	1	1

INFRATENTORIAL	CC	DAWSON_F	Ce	BRAIN STEM	BG	THALAMUS	SIZE_LES	GADO	CERVICAL	Cerebral atrophy type	F/U MRI after	Improvement	Atrophy
2	1	1	2	2	2	2	1	2	2	4	2	3	2
2	2	2	2	1	2	2	1	2	1	4	0.2	0	2
1	1	2	1	1	1	1	1	1	1	2	0	0	1
1	1	1	1	1	2	2	1	2	1	2	1	0	1
1	2	2	1	1	2	2	1	1	1	2	2	3	1
2	2	2	2	2	2	2	1	1	1	4	0	0	2
1	1	2	1	1	1	2	1	2	1	2	1	1	1
1	1	2	1	1	2	1	1	1	1	4	3	1	2
1	2	2	2	1	2	2	1	2	1	4	0	0	2
2	1	1	2	2	2	2	1	2	1	4	0	0	2
1	1	1	1	1	2	2	1	1	1	4	0.5	3	2
2	1	1	2	2	2	2	1	2	1	2	7	3	1
2	1	1	2	2	2	2	1	1	1	4	3	2	2
2	1	2	2	2	2	2	1	2	1	4	0.4	3	2
2	2	2	2	1	2	2	1	2	1	4	1	3	2
1	1	1	1	1	2	2	2	1	2	2	3	2	1
2	1	2	2	2	2	2	1	2	1	4	4	3	2
1	2	2	2	2	2	2	1	1	1	2	0.4	2	1
1	1	2	2	1	2	2	1	2	2	2	3	3	1
1	2	2	2	1	1	2	2	2	1	4	0	0	2
2	2	2	2	2	2	2	1	2	2	2	5	3	1
2	1	1	2	2	2	2	1	2	1	4	1	3	2
1	2	2	2	1	1	2	1	2	1	4	0.5	3	2
1	2	2	1	1	1	1	1	2	1	4	1	2	2
1	1	1	2	1	2	2	1	2	2	2	0.5	3	1
1	1	1	2	1	1	1	1	2	2	2	1	2	1
2	1	2	2	1	2	2	1	1	1	2	1	2	1
2	1	2	2	2	2	2	1	2	1	4	0	0	2
1	2	2	2	1	2	2	2	2	2	2	0	0	1
2	2	2	2	2	2	2	1	2	1	2	2	2	1
2	2	2	2	2	2	2	1	1	1	4	0.4	1	2
1	1	1	2	2	2	2	1	2	1	5	8	2	1
1	1	2	2	2	2	2	1	2	1	5	0	0	1
1	1	1	1	1	2	2	1	1	1	5	1	2	1
1	2	2	2	2	2	2	1	1	1	5	2	2	1
1	2	2	1	1	1	2	1	2	1	2	7	2	1
1	2	2	1	1	2	1	1	2	2	2	2	3	1
1	2	2	2	1	2	1	1	1	1	4	1	1	2
1	2	2	1	1	2	2	1	1	1	4	3	3	2
1	2	2	2	1	2	2	1	2	1	5	0	0	1

INFRATENTORIAL	CC	DAWSON_F	Ce	BRAIN STEM	BG	THALAMUS	SIZE_LES	GADO	CERVICAL	Cerebral atrophy type	F/U MRI after	Improvement	Atrophy
2	2	2	2	2	2	2	1	2	1	2	3	3	1
1	2	2	2	1	2	2	1	2	2	4	0	0	2
2	2	2	2	1	2	2	1	2	1	2	2	2	1
1	1	1	2	1	2	1	1	2	2	2	3	2	1
2	1	1	2	2	2	2	1	2	1	4	0	0	2
1	1	1	2	1	2	2	1	2	1	2	8	2	1
1	2	2	2	1	1	1	1	2	1	2	1	2	1
1	2	2	2	1	1	2	1	2	1	4	0	0	2
2	2	2	2	2	2	2	1	2	1	2	0	0	1
2	1	2	2	2	2	2	1	2	2	4	1	3	2
1	2	2	2	1	2	2	1	2	1	5	1	2	1
2	1	1	2	2	2	2	1	2	2	2	1	2	1
1	1	1	2	1	1	2	1	1	1	2	3	2	1
2	2	2	2	2	2	2	1	2	2	2	1	3	1
2	2	2	2	2	2	2	1	2	2	4	1	3	2
1	2	2	1	1	2	2	1	2	1	4	4	2	2
1	1	2	2	1	1	1	1	2	2	4	0	0	2
2	1	2	2	1	2	1	1	2	1	2	3	2	1
2	1	1	2	2	2	2	1	2	2	4	1	3	2
1	2	2	2	1	2	2	1	2	2	2	0	0	1
1	2	2	1	1	2	1	1	2	1	5	0	0	1
1	2	2	2	1	2	1	1	2	1	4	0	0	2
2	2	2	2	2	2	2	1	1	1	2	0	0	1
1	1	2	2	2	1	2	1	2	1	4	3	2	2
1	1	1	1	2	2	1	1	2	2	2	3	3	1
1	1	1	1	2	2	2	1	2	1	2	0	0	1
1	1	1	1	2	2	2	1	2	1	4	0	0	2
2	1	1	2	2	2	2	2	2	1	2	1	3	1
1	1	1	1	1	2	2	1	2	1	2	0	0	1
2	1	1	2	2	2	2	1	2	2	4	0	0	2
1	1	1	2	1	2	1	1	2	1	4	0	0	2
1	1	2	2	1	1	1	1	2	1	2	1.6	2	1
2	2	2	2	2	2	2	1	2	1	2	0	0	1
1	1	1	2	1	1	1	1	2	1	2	2	3	1
1	1	1	2	1	2	2	1	2	1	5	0	0	1
1	2	2	1	1	1	1	1	2	1	5	0	0	1
1	1	2	1	1	1	2	1	2	1	4	0.5	1	2

Sl. No	M.Predni	Pulse MP	AZT	MMF	Mitaxan	INF	Cyclopho	Follow U	F/U Durat
1	1	1	2	1	2	2	2	1	9
2	1	1	2	1	1	2	1	1	20
3	1	3	1	2	2	2	2	1	20
4	2	2	2	1	2	2	2	1	3
5	1	2	2	1	2	2	2	1	2
6	1	2	1	2	2	2	2	1	15
7	1	1	2	2	2	2	1	1	6
8	1	1	2	2	2	2	1	1	6
9	1	1	2	1	2	2	2	1	9
10	1	1	2	1	2	1	2	1	1
11	1	1	2	1	2	2	2	1	2
12	1	3	1	2	2	2	2	1	9
13	1	1	2	1	2	1	2	1	7
14	2	1	1	1	2	2	2	1	8
15	2	1	2	2	2	2	1	1	4
16	2	2	1	2	2	2	2	2	0
17	2	1	2	1	2	2	2	1	2
18	1	3	2	1	2	2	2	1	5
19	2	1	2	1	2	2	2	1	9
20	1	2	2	1	2	2	2	1	5
21	1	2	1	1	2	1	2	1	24
22	1	2	1	2	2	2	2	1	14
23	1	1	2	1	2	2	2	1	1
24	1	1	1	2	2	2	1	1	15
25	1	2	1	2	2	2	2	1	12
26	1	1	2	1	2	2	2	1	4
27	1	1	2	1	2	2	2	1	2.5
28	1	1	2	1	2	2	1	1	18
29	1	3	2	1	2	2	2	1	10
30	1	2	1	2	2	2	2	1	12
31	1	1	2	1	2	2	2	1	7
32	1	1	2	1	2	2	2	1	33
33	1	1	1	1	2	2	2	1	9
34	1	2	1	2	2	2	2	1	8
35	1	2	2	1	2	2	2	1	8
36	1	1	2	1	2	2	2	1	8
37	1	3	2	1	2	2	2	1	6
38	1	2	1	2	2	2	2	1	14
39	1	1	2	1	2	2	2	1	3
40	1	2	1	2	2	2	2	1	3

Sl. No	M.Predni	Pulse MP	AZT	MMF	Mitaxan	INF	Cyclopho	Follow U	F/U Durat
41	1	1	2	2	2	2	1	1	22
42	1	1	2	1	2	2	2	1	11
43	1	1	2	1	2	2	2	1	3
44	1	1	2	1	2	2	1	1	5
45	1	1	2	1	2	2	2	1	2
46	1	2	1	1	2	2	2	1	8
47	1	1	2	1	2	2	2	1	9
48	1	1	2	1	2	2	2	1	13
49	1	1	2	1	2	2	2	1	3
50	1	1	2	2	2	1	1	1	12
51	1	1	2	1	2	2	2	1	1
52	1	2	1	2	2	2	2	1	6
53	1	2	1	2	2	2	2	1	10
54	1	1	2	1	2	2	2	1	3
55	1	2	2	1	2	2	2	1	19
56	1	1	2	1	1	2	2	1	3
57	1	1	1	1	2	2	2	1	4
58	1	1	2	1	2	2	2	1	4
59	1	1	2	2	2	2	1	1	5
60	1	1	2	2	2	2	1	1	8
61	1	1	1	1	2	2	2	1	7
62	1	2	1	1	2	1	2	1	16
63	1	1	2	1	2	2	2	1	5
64	1	1	2	1	2	2	2	1	6
65	1	1	2	1	2	2	2	1	2
66	1	1	2	2	2	2	1	1	7
67	1	2	2	2	2	2	2	2	0
68	1	1	2	1	2	2	2	1	25
69	1	1	1	1	2	2	2	1	5
70	1	1	2	1	2	2	2	1	2
71	1	2	1	2	2	2	2	2	0
72	1	1	1	2	2	2	2	1	6
73	1	1	2	1	2	2	2	1	3
74	1	2	2	1	2	2	2	1	6
75	1	1	2	1	2	1	2	1	3
76	1	3	2	1	2	2	1	1	11
77	1	1	2	1	2	2	2	1	3
78	1	1	2	1	2	2	1	1	5
79	1	1	2	1	2	2	2	1	6
80	1	1	2	1	2	2	2	1	4

Sl. No	M.Predni	Pulse MP	AZT	MMF	Mitaxan	INF	Cyclopho	Follow U	F/U Durat
81	1	1	2	1	2	1	2	1	8
82	1	2	2	2	2	2	1	1	4
83	1	1	2	1	2	2	2	2	0
84	1	2	2	2	2	1	2	1	18
85	1	3	2	1	2	2	2	1	9
86	1	2	2	1	2	2	2	1	4
87	1	1	2	1	2	2	1	1	9
88	2	3	2	1	2	2	2	1	9
89	1	2	1	2	2	2	2	1	9
90	1	2	1	2	2	2	2	2	0
91	1	2	2	1	2	2	2	1	13
92	1	1	1	1	2	2	1	1	22
93	1	2	1	2	2	2	2	1	11
94	1	2	1	2	2	2	2	2	0
95	1	2	1	2	2	2	2	2	0
96	2	3	1	1	2	2	2	1	8
97	1	2	1	2	2	2	2	2	0
98	1	2	1	2	2	2	2	2	0
99	1	2	1	2	2	2	2	2	0
100	1	2	2	1	2	2	2	2	0
101	1	2	1	2	2	2	2	1	8
102	1	2	1	2	2	2	2	2	0
103	1	2	2	2	2	2	2	2	0
104	1	1	2	1	2	2	2	1	6
105	1	2	1	2	2	2	2	1	9
106	1	2	1	2	2	2	2	1	7
107	1	2	2	2	2	1	1	1	7
108	1	2	1	2	2	2	2	2	0
109	1	2	1	2	2	2	1	2	0
110	1	2	1	1	2	2	2	1	8
111	2	3	2	1	2	2	2	1	4
112	1	2	1	1	2	2	2	2	0
113	1	2	2	1	2	2	2	2	0
114	1	1	2	1	2	2	2	1	15
115	1	1	1	2	2	2	2	1	6
116	1	3	2	1	2	2	2	2	0
117	1	1	2	1	2	2	1	1	5
118	1	1	2	1	2	2	1	1	3
119	1	3	2	1	2	2	2	2	0
120	1	1	2	2	1	2	2	2	0

Sl. No	M.Predni	Pulse MP	AZT	MMF	Mitaxan	INF	Cyclopho	Follow U	F/U Durat
121	1	2	2	1	2	2	2	1	8
122	1	1	2	1	2	2	2	1	1
123	1	2	1	2	2	1	1	2	0
124	1	3	1	2	2	2	2	2	0
125	1	2	1	2	2	2	2	2	0
126	1	1	1	2	1	2	1	1	19
127	1	2	1	2	2	2	2	2	0
128	1	2	1	2	2	2	2	2	0
129	1	2	1	2	2	2	2	2	0
130	1	2	1	2	2	2	2	2	0
131	2	2	1	2	2	2	2	2	0
132	1	2	1	2	2	2	2	2	0
133	1	2	2	2	2	2	2	2	0
134	1	2	1	2	2	2	2	2	0
135	1	2	1	2	2	2	2	2	0
136	1	2	1	2	2	2	2	2	0
137	1	2	1	2	2	2	2	2	0
138	1	2	1	2	2	2	2	1	17
139	1	2	2	1	2	2	2	2	0
140	1	2	1	2	2	2	2	1	15
141	1	2	1	2	2	2	2	2	0
142	1	2	1	2	2	2	2	2	0
143	1	2	1	2	2	2	2	1	5
144	1	2	1	2	2	2	2	1	13
145	1	2	2	1	2	2	2	2	0
146	1	3	2	1	2	2	2	1	7
147	1	2	1	1	1	2	2	1	8
148	1	2	2	2	2	1	2	1	10
149	1	2	1	2	2	2	2	1	9
150	1	1	2	1	2	2	2	1	4
151	1	1	2	1	2	2	2	2	0
152	1	1	2	1	2	2	2	1	5
153	1	2	1	2	2	1	2	1	17
154	1	1	2	2	2	1	2	2	0
155	1	2	1	2	2	2	2	2	0
156	1	2	1	2	2	2	2	2	0
157	1	2	1	2	2	2	2	2	0

MASTER CHART

Abbreviations

Complete Recovery from 1st episode yes- 1

Incomplete recovery-2

Gender- Male-1

Female-2

RR-1, PP-2, SP-3, PR-4
Presentation------ Monophasic-1 poly phasic-2
Male-1 female-2

Acute onset < 7 days- 1, sub acute onset 7 days to 1 month-2, chronic >1 month- 3

Acute-1, subacute-2, chronic-3, Ac+subacute-4, Acute+Subacute+chr-5, Subacute+Chronic-6, Acute+chronic-7

Presenting symptom-Visual U/L-1,B/L-2,None-3
Presenting symp Motor-Monoparesis-1, paraparesis-2, quadriparesis-4, hemiparesis-5 none-6
YES-1 no- 2
Monosymptomatic-1, polysymptomatic-2
CSF protein < 45- 1, 45-90-2, 90-135-3, >135-4

CSF Cells <10-1, 10-25-2, 25-50-3, >50-4

VEP normal -1, U/L abnormal- 2, B/L abnormal-3, not done-4, data not available-5

SSEP median normal-1, abnormal- 2, not done-3, data not available-5

MRI no of lesions- <5-1, 6-10-2, 11-15-3, >15-4

Size of lesions- <3 cm- 1, 3-5 cm- 2, <5 cm-3

MRI improvement-1, worsening- 2, status quo- 3

MRI spinal segments< 3- 1, >3-2

OCB present-1, absent-2, data not available-3